VOL. CLXVII, No. 5 MAY, 1924 No. 626

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

JOHN H. MUSSER, JR., M.D., EDITOR
E. B. KRUMBHAAR, M.D., ASSOCIATE EDITOR

THE LIBRARY OF CONGRESS SERIAL RECORD
JUL 26 1924

ESTABLISHED 1820

EXPERIMENTAL STUDIES IN ELECTROIONIC MEDICATION. By GEORGE T. PACK, M.D., FRANK P. UNDERHILL, PH.D., JOSEPH EPSTEIN, M.D., and I. NEWTON KUGELMASS, PH.D. 625

STUDIES IN PANCREATIC FUNCTION. THE ENZYMIC CONCENTRATIONS OF DUODENAL CONTENTS IN HEALTH AND DISEASE By C. W. MCCLURE, M.D., with the collaboration of CHESTER M. JONES, M.D., A. S. WETMORE, and LAWRENCE REYNOLDS, M.D. 649

THE OCCURRENCE OF REGULAR VENTRICULAR RHYTHM WITH A RATE OF OVER FIFTY IN CASES OF AURICULAR FIBRILLATION. By W. DOCK, M.D., and S. A. LEVINE, M.D. 664

RIGHT DIAPHRAGMATIC HERNIA OF THE SHORT ESOPHAGUS TYPE. By SOLOMON FINEMAN, M.D., and H. MILTON CONNER, M.D. 672

THE HYPOPHYSEOBASAL AREA IN ITS RELATION TO THE PATHOGENESIS AND TREATMENT OF DIABETES INSIPIDUS AND POLYURIA (INCLUDING A STUDY OF THIRTY AUTOPSIES). By CHARLES E. DE M. SAJOUS, M.D., LL.D., SC.D. 679

CEREBROSPINAL FLUID IN ENCEPHALITIS LETHARGICA. By HAROLD E. FOSTER, M.D., and JESSIE REED COCKRELL, A.B. 696

A POSSIBLE RELATIONSHIP BETWEEN THE CURRENT OF INJURY AND THE WHITE-BLOOD CELL IN INFLAMMATION. By HAROLD A. ABRAMSON, M.D. 702

PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF PATIENTS PRESENTING ESSENTIAL HYPERTENSION. By ERNEST S. DU BRAY, M.D. 710

LEUKEMIA: REPORT OF AN ATYPICAL CASE. By BENJAMIN GUTMANN, M.D. . . . 718

THE RELATIONSHIP OF GOITER TO MENTAL DISORDERS. By HAROLD L. FOSS, M.D., and J. ALLEN JACKSON, M.D. 724

A STUDY OF THE ULTRAVIOLET ABSORPTION SPECTRA OF CEREBROSPINAL FLUID—A NEW TEST (PRELIMINARY REPORT). By TAKUJI SHIONOYA, M.D. 735

INDEX TO ADVERTISERS . . . . . ADV. PAGE 35

Contents continued on page x

OWNERS AND PUBLISHERS
Philadelphia LEA & FEBIGER New York

COPYRIGHT, 1924, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, SIX DOLLARS A YEAR, POSTPAID

D&G 20-Day Catgut

Reductions in Prices *of D&G Sutures*

Standard Tubes for Major Surgery—
Reduced to **$2.40** Dozen; **$25.92** net per Gross.
(Formerly $3.00 dozen; $27.00 net per Gross)

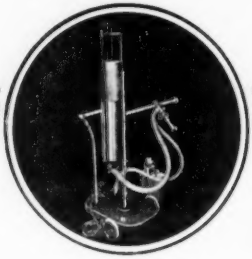
Short Sutures for Minor Surgery—
With Needles: **Reduced to $1.80 dozen** (formerly $3.00).
Without Needles: **Reduced to $1.20 dozen** (formerly $1.50).
Effective May First

The Purpose of D&G
is to make the best sutures that can be made and to sell them at a fair price

Send for interesting new booklet of complete information

DAVIS & GECK, INC.
Surgical Sutures Exclusively
211-221 Duffield Street ~ Brooklyn, N.Y., U.S.A.

COPYRIGHT MAY 1924 D&G INC.



You will find the Sanborn Benedict a trustworthy medium for accurate basal metabolism determinations in your laboratory.

An apparatus for the specialist, who must transmit his routine work to an assistant. Simple, sturdy construction, assuring accuracy at all times, even in the hands of an untrained technician.

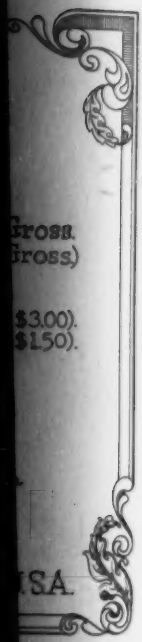
Our directions—the metabolism test from beginning to end—are complete. Ask for description 5J. Sanborn Co., 1048 Commonwealth Avenue, Boston.

SANBORN
DIAGNOSTIC APPARATUS

A

IL

This
made
sultin
impr
methe
It is
share
and
availa



ANOTHER REDUCTION IN THE PRICE OF

ILETIN (INSULIN, LILLY)

TO PHYSICIANS

Effective March 15th, the price of Iletin to physicians was reduced as follows:

U-10— 50 units (10 units per c.c.) from $1.10 to $ .90
U-20—100 units (20 units per c.c.) from $2.00 to $1.50
U-40—200 units (40 units per c.c.) from $3.75 to $2.80

THIS REDUCTION in price has been made possible through economies resulting from increased production and improvements in manufacturing methods.

IT IS IN KEEPING with our desire to share these savings with the consumer and to make Iletin (Insulin, Lilly) available to every diabetic at the lowest possible price consistent with the highest quality and a reasonable manufacturer's profit.

WHOLESALE and retail druggists throughout the United States are now generally stocked and no difficulty should be found in obtaining Iletin (Insulin, Lilly) from your customary source of supply.

Send for Pamphlet Giving Full Information

ELI LILLY AND COMPANY

INDIANAPOLIS, INDIANA, U.S.A.

NEW YORK CHICAGO SAINT LOUIS KANSAS CITY NEW ORLEANS

Yeast

an established prescription of the general practitioner

ALTHOUGH for centuries yeast has been prescribed by physicians, it has been notably in the past seven years that scientific research has revealed new and extended fields for its use.

During this period exhaustive investigations have been carried out under independent authorities. In all, six separate groups of men have completed rigidly conducted tests and experimental work on the various phases of yeast's activity.

Summarized, the aggregate findings of the different groups of scientists engaged on this research work are as follows:

First: The water soluble B-vitamin, of which yeast is the richest source extant, raises the plane of metabolism rapidly and effectively — indicating yeast as a simple corrective for digestive troubles, and an extremely valuable dietary aid.

Second: By inducing a leucocytosis yeast provides a highly efficacious treatment of furunculosis and other skin disorders.

Third: The laxative action of yeast not only produces an increase in the bulk and moisture of the feces and (to quote the findings of the most recent investigation) an "improvement in the condition of every individual" with "any degree of constipation" but also acts as a natural, efficient bowel regulator without any drastic purgative action.

The combination of these three properties makes yeast a valuable prescription not only in cases of specific trouble but also in certain cases of vague ill health which require a restorative for the general tone of the system.

Fleischmann's Yeast can be taken dissolved in milk or fruit juices or eaten plain. A popular method of administration is one cake half an hour before breakfast and the last thing at night dissolved in a glass of water (just hot enough to drink).

New brochure on yeast therapy sent on physician's request

THE FLEISCHMANN COMPANY, Dept. K-31
701 Washington Street, New York.

Please send me free a copy of the brochure on yeast based on the published findings of distinguished investigators.

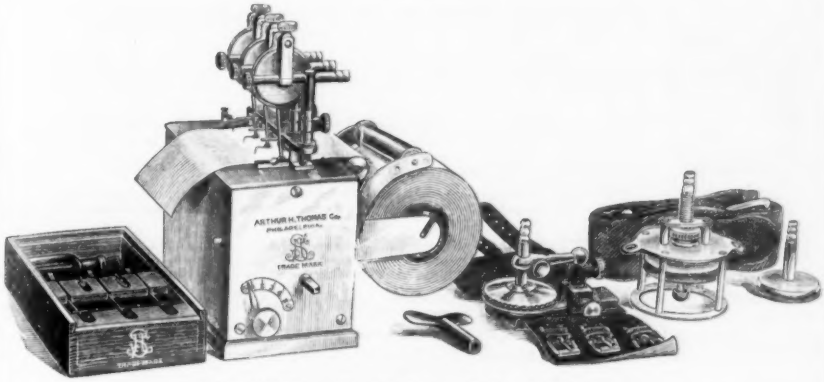
Name.....

Street.....

City.....State.....

JAQUET
PORTABLE POLYGRAPH

THE TEST
IN OUR STOCK FOR IMMEDIATE SHIPMENT
OF SERVICE



No. 3610 Jaquet Portable Polygraph, Complete Outfit

JAQUET PORTABLE POLYGRAPH, New Model, an instrument of great precision and convenience, by many considered the most sensitive mechanical device for the graphic study of the circulation. With it three simultaneous tracings are recorded, either in ink or on smoked paper, *i.e.*, radial pulse, apex beat and one other, such as carotid, jugular, etc., in addition to time tracing.

Tracings can be made to any desired length from a continuous roll of paper, and at any speed from 2 mm to 50 mm per second. The clockwork is of the highest precision, marking time in either 1 or 1/5th second, and runs for 25 minutes at the lowest speed of 1 cm per second.

A recent improvement in the sphygmograph attachment for radial pulse permits the attachment of the wrist-band with the receiving tambour removed in order conveniently to locate the radial pulse exactly in the open space of the wrist-band, after which the receiving tambour of the sphygmograph can be quickly attached in exactly the correct position. The workmanship and finish are such as are embodied in no other instrument for similar purposes.

3610. **Jaquet Portable Polygraph,** as above described, with set of pens for both ink and smoked paper tracings, sphygmograph for radial pulse, cardiograph for apex beat, receiver for carotid, jugular, etc., and one roll each of glazed and smoked paper..... $200.00

Code Word ..... *Doabr*

Price subject to change without notice

ARTHUR H. THOMAS COMPANY

RETAIL—WHOLESALE—EXPORT

LABORATORY APPARATUS AND REAGENTS

WEST WASHINGTON SQUARE PHILADELPHIA, U. S. A.

CABLE ADDRESS, "BALANCE," PHILADELPHIA

CHEPLIN'S B. ACIDOPHILUS MILK

(Produced under the direct supervision of Harry A. Cheplin, Ph.D.)

FOR

INTESTINAL TOXEMIA

14-oz. bottles
A. M. A.
Council Accepted

CHEPLIN'S B. ACIDOPHILUS MILK will be found of distinct value in the treatment of intestinal toxemias. It provides an effective means of overcoming putrefactive processes in the intestines and regulating bowel movements.

Clinical improvement is manifested by relieving co-existing toxic symptoms of headache, fatigue and intestinal gas.

A bacteriological simplification of the intestinal flora results and the pernicious toxicogenic microbes are replaced by the beneficial acidophilus bacilli.

DOSAGE—For adults, 14-21 ounces daily in 7-oz. doses (one tumblerful), for at least 6 weeks. The addition of one to three tablespoonfuls of lactose per dose is important in obstinate cases.

The following points deserve particular emphasis:

CULTURE: Contains approximately 250,000,000 viable and potent acidophilus bacilli per c.c. Physicians who subjected it to a bacteriological test have recognized its superior quality.

SERVICE: Culture is shipped direct to physicians or their patients by express or parcel post on the day of receipt of order. Arrangements can be made whereby weekly shipments will go forward regularly, thus insuring a continuous and fresh supply.

VOLUME: The large size, 14-OUNCE bottles, which we use contain 400 c.c. or 2 tumblersful. This represents the minimum requisite amount of culture per day.

PRICE: SIX 14-oz. BOTTLES, $2.00; TWELVE 14-oz. BOTTLES, $3.75, plus delivery charges

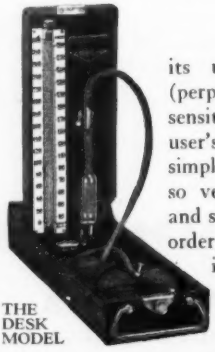
FULL INFORMATION, REFERENCES TO PUBLICATIONS AND PHYSICIAN'S SAMPLE UPON REQUEST

CHEPLIN BIOLOGICAL LABORATORIES, INC. - - SYRACUSE, N. Y.

TENS OF THOUSANDS NOW USE THE Baumanometer

"STANDARD FOR BLOODPRESSURE"

BECAUSE



THE DESK MODEL

its unvarying accuracy (perpetually guaranteed), sensitive response to the user's will, and that utter simplicity which makes it so very easy to operate and so hard to get "out of order," combine to make it the splendid, serviceable instrument which users know it to be.

DESK MODEL . . . 300 mm. calibration	$32.00
KIT-BAG MODEL . . 260 mm. calibration	$31.00
POCKET MODEL . . 200 mm. calibration	$30.00
WALLBOARD MODEL 300 mm. calibration	$28.00

SUPPLIED THROUGH YOUR DEALER

W. A. BAUM CO., INC. - 100 FIFTH AVENUE - NEW YORK

Gastron

The entire-stomach-gland extract

Submitted to the physician as a resource against gastro-intestinal affections.

Gastron presents the complex proteins, coagulable and non-coagulable, the nucleo-proteins, amino-acids, etc., derivable from the gastric mucosa.

Agreeable solution—no sugar, no alcohol.

Fairchild Bros. & Foster
New York

TOLYSIN

CONGESTIVE CONDITIONS
NERVOUS HEADACHES
PAINFUL MENSTRUAL CONDITIONS

respond quickly to the analgesic and antipyretic action of TOLYSIN. It is well tolerated. TOLYSIN exerts its action in the intestines. Usual dosage is 2–3 tablets (10–15 grains) three to four times daily with water. Boxes of 20 and 50 tablets.

Tolysin literature on request

Calco

THE CALCO CHEMICAL COMPANY
Pharmaceutical Division
Bound Brook, N. J. **New York, N. Y.**

FOR CONTROL OF PAIN AND INSOMNIA

CONSIDER

ALLONAL "Roche"

INSTEAD OF NARCOTICS

Many medical reports declare its great value in Insomnia, with and without pain,—Carcinoma—Neuritis—Neuralgias—tic-douloureux—Tabetic pains—Sciatica—Pre- and Post-operative sedative. It has also been found very useful in the treatment of Narcotic Addiction and Alcoholism.

Allonal possesses the combined sleep-producing and pain-allaying properties of the opiates—and yet it is non-narcotic.

Physicians are saying that Allonal is enabling them to get along with less of the narcotics.

DOSAGE: *For Insomnia, 1 to 2 tablets*
For Control of Pain, 2 to 4 tablets

Bottles of
12 and 50 Tablets (2⅔ grs.)

The HOFFMANN-LA ROCHE CHEMICAL WORKS
New York

CÉLESTINS
VICHY

The place of CÉLESTINS Vichy in the dietary is distinctive and important. It is an alkaline water of diuretic action, and is indicated in cases of the following:

Chronic hepatic disorders; gastric and intestinal indigestions; acid dyspepsia; chronic catarrhal gastritis or enteritis; rheumatism; diabetes; inflammation of the bladder; and a large number of minor ailments.

CÉLESTINS VICHY is bottled only at Vichy, France, under the direct supervision of the French Government. Order and insist upon getting CÉLESTINS VICHY.

A booklet on the therapeutic uses of CÉLESTINS Vichy will be sent on request.

HENRY E. GOURD

General Distributor

456 Fourth Avenue **New York City**

New Castle Incubator

CASTLE

Chamber has uniform and constant temperature

THE new Castle incubator fills the need for a reliable and accurate apparatus at a moderate price.

The electric heater is beneath the bottom (not taking up space in the chamber). It distributes the heat uniformly from the bottom to the top and maintains an unvarying temperature.

The automatic regulator controls the escape of excess heat up and out through the rear double wall. The walls are made of thick insulating material, bound with polished copper.

Send for details and prices

CASTLE

Sterilizers and bacteriological apparatus

Wilmot Castle Co., 1160 University Av., Rochester, N. Y.

YOU can use this Convertible Substage Lamp with both a dark-ground illuminator and an Abbe Condenser. The change between the two is easily made, so that you have at your disposal a powerful and convenient light source for both dark-field microscopy and oil-immersion work. Write for booklet describing the

Bausch & Lomb
CONVERTIBLE
SUBSTAGE LAMP

Bausch & Lomb Optical Co.

Desk E 31, 635 St. Paul Street, Rochester, N. Y.

NEW YORK WASHINGTON CHICAGO SAN FRANCISCO LONDON

D.R.L.

Achievements

Under the direction of Dr. George W. Raiziss, the chemists of The Dermatological Research Laboratories have developed for the American profession, the following notable products:

Arsphenamine, D. R. L.

First produced to meet the urgent wartime needs of the U. S. Government. For effectiveness-with-safety a drug of acknowledged superiority, the result of continued research and refinements in method of manufacture.

Neoarsphenamine, D. R. L.

Exceeding Government requirements from 50 to 75%, based on official toleration tests. Affords a wide margin of safety for the patient while yet possessing a trypanocidal activity practically equal to that of Arsphenamine. The choice of eminent syphilogists everywhere.

Sulpharsphenamine, D. R. L.

For intramuscular use. For patients with small or inaccessible veins, in neurosyphilis, or other instances when this appears to be the arsenical of choice, physicians are urged to employ this reliable American-made brand, the first to be made in this country.

Potassium Bismuth Tartrate with Butyn, D. R. L.

By many, considered superior to mercury in general syphilotherapy, and used by them as a routine measure in place of mercury and in connection with Neoarsphenamine. Useful in all cases and particularly so for arsenic-resistant patients and in relapsing and unresponsive tertiary cases. Injections practically painless.

Metaphen, D. R. L.

A new organic mercury compound more powerful yet less toxic than bichloride. Also non-irritant and so may be used upon mucous as well as cutaneous surfaces (in urethritis, etc.). Quickly sterilizes hands, instruments and glassware. *Does not stain.*

Ask your Dealer for D. R. L.

Distilled water free with certain sizes of **Neoarsphenamine** and **Sulpharsphenamine.**

Arsphenamine, Neoarsphenamine and Sulpharsphenamine made under license from The Chemical Foundation, Inc.

The Dermatological Research Laboratories

1720-22 Lombard St., Philadelphia, Pa.

The Abbott Laboratories

4757 Ravenswood Avenue, Chicago, Ill.

New York Seattle San Francisco

SAFETY FIRST
QUALITY ALWAYS

THE "SPA"
DIET HOSPITAL

WAUKESHA, WIS.

For the Treatment of

DIABETES

BRIGHT'S DISEASE *and*

HIGH BLOOD PRESSURE

Iletin (Insulin-Lilly) used in Diabetes when Indicated

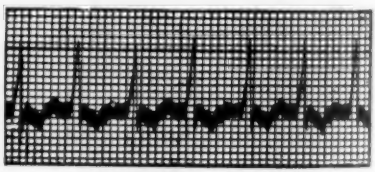
Write for Booklet

THE "SPA" - - WAUKESHA, WIS.

"ELECTROCARDIOGRAPHY

Furnishes definite, indisputable evidence of structural heart muscle defect that is impossible of determination by any other method of examination."

S. CALVIN SMITH



A positive confirmation of the diagnosis.
WHAT IS IT?

Practitioners, clinics and hospitals find it essential for a complete examination and the returns capable of creating its own maintenance fund besides allowing a generous surplus each year.

Catalog and details on request

The Cambridge and Paul
INSTRUMENT Co. of AMERICA (Inc)

MAIN OFFICE AND FACTORY OSSINING-ON-HUDSON NEW YORK | INCORPORATING CHAS. F. HINDLE | SALES OFFICE & SHOWROOM GRAND CENTRAL TERMINAL NEW YORK CITY

Lessens Danger *of* DIARRHEA *in* Infant Feeding

A RECENT REPORT of leading pediatrists emphasizes the fact that Karo (Corn Syrup) is peculiarly adaptable to modifying fresh cow's milk for infant feeding, and is less likely to cause Diarrhea.

PATIENTS should be instructed to ask simply for Karo, the Corn Syrup which, for the past 20 years, has been sold by grocers throughout America.

TO THE PROFESSION: The composition of Karo (Corn Syrup) and information for Infant Feeding gladly furnished on request. Corn Products Refining Co., 17 Battery Place, New York City.

CONTENTS

ORIGINAL ARTICLES

Experimental Studies in Electroionic Medication 625

By George T. Pack, M.D., Frank P. Underhill Ph.D., Joseph Epstein, M.D., and I. Newton Kugelmass Ph.D. New Haven, Conn.

Studies in Pancreatic Function. The Enzymic Concentrations of Duodenal Contents in Health and Disease 649

By C. W. McClure, M.D. with the collaboration of Chester M. Jones, M.D., A. S. Wetmore and Lawrence Reynolds, M.D., Boston, Mass.

The Occurrence of Regular Ventricular Rhythm with a Rate of Over Fifty in Cases of Auricular Fibrillation 664

By W. Dock, M.D. and S. A. Levine M.D., Boston.

Right Diaphragmatic Hernia of the Short Esophagus Type 672

By Solomon Fineman, M.D., and H. Milton Conner, M.D., Rochester, Minn.

The Hypophyseobasal Area in its Relation to the Pathogenesis and Treatment of Diabetes Insipidus and Polyuria (Including a Study of Thirty Autopsies) 679

By Charles E. de M. Sajous, M.D., LL.D., Sc.D., Philadelphia.

Cerebrospinal Fluid in Encephalitis Lethargica 696

By Harold E. Foster, M.D., Rochester, N. Y., and Jessie Reed Cockrell, A.B., Boston, Mass.

A Possible Relationship between the Current of Injury and the White-Blood Cell in Inflammation 702

By Harold A. Abramson, M.D., New York.

Practical Considerations in the Management of Patients Presenting Essential Hypertension 710

By Ernest S. du Bray, M.D., Los Angeles, Calif.

Leukemia: Report of an Atypical Case 718

By Benjamin Gutmann, M.D., New Brunswick, N. J.

The Relationship of Goiter to Mental Disorders 724

By Harold L. Foss, M.D., and J. Allen Jackson, M.D., Danville, Pa.

A Study of the Ultraviolet Absorption Spectra of Cerebrospinal Fluid—a New Test (Preliminary Report) 735

By Takuji Shionoya, M.D., Tokio, Japan.

(Contents continued on page 12)

ORGANOTHERAPY

can be effective only through the use of dependable endocrine products. A proper manufacturing process is absolutely indispensable.

> "* * * every link in the manufacture of the glandular substance plays a vital part in its future therapeutic value, every stage in its production counts in its efficiency. It may become either a dangerously potent weapon or an inert mass." — ("Our Problems in Endocrinology," Jacob Gutman, M.D., Phar.D., F.A.C.P., Chairman's address to the Endocrinological Society of the City of New York, 1922.)

Our products are prepared from fresh glands of healthy food animals in our own laboratory, under the supervision of our own staff of chemists. Every manufacturing process has been carefully tested and every product for which there is a recognized chemical or biological assay is analyzed and standardized.

EPINEPHRINE
EPINEPHRINE CHLORIDE SOL.
DESICCATED PITUITARY BODY, U. S. P.
DRIED SUPRARENALS, U. S. P.
DRIED THYROIDS, U. S. P.
SOLUTION OF POST-PITUITARY
CORPUS LUTEUM
PANCREATIN, U. S. P.

Insure potency and constancy of action by prescribing the products of

G. W. CARNRICK CO.

Manufacturers of G.W. CARNRICK CO. **Organotherapeutic Products**

417-421 Canal Street, New York, N. Y.

REVIEWS

Local Anesthesia: Its Scientific Bases and Practical Use. By Prof. Dr. Henrich Braun; translated and edited by Malcolm L. Harris, M.D. 748
Modern Urology. In Original Contributions by American Authors. Edited by Hugh Cabot, M.D., C.M.G., F.A.C.S. 749
Intranasal Surgery. By J. A. Pratt, M.D. 750
Practical Chemical Analysis of Blood. By Victor Caryl Myers M.A., Ph.D. 750
Intravenous Therapy. By Walton Forest Dutton M.D. 750
Pediatrics. By Various Authors. Edited by Isaac A. Abt, M.D. . . . 751
Forty-three Grafts from Monkey to Man. By Serge Voronoff 755
Walter Reed and Yellow Fever. By Howard A. Kelly, M.D. 756
Excursions into Surgical Subjects. By John B. Deaver, M.D., ScD., LL.D., F.A.C.S., and Stanley P. Reimann, M.D. 756

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

The Staining of Treponema Pallidum in Dry Smears 757
Treatment of Myeloid Leukemia with Thorium X 758
An Analysis of the Clinical Histories of Patients with Pernicious Anemia in the Johns Hopkins Hospital from 1918 to 1922 Inclusive . . . 758
On the Phosphorus and Calcium of the Blood in Renal Disease . . . 759
Bacteriological Observations on Acute Tonsillitis with Reference to Epidemiology and Susceptibility 759
Gonorrheal Myelitis 760
Two Cases of Canine Tuberculosis Caused by Human Tubercle Bacilli . 760
Local Vaccination of the Intestine Against Dysentery 760

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

Treatment of Hypertrophic Pyloric Stenosis 761
Surgical Treatment of Unilateral Pulmonary Tuberculosis 761
Carcinoma of the Colon 761
Urinary Antiseptics 762
Experimental Closure of Large Bronchi 762
Operation Shock 762
Case of a Retroperitoneal and Perinephric Infection (Abscess) Treated by Intravenous Injection of Mercurochrome 762
Diverticulum of the Urinary Bladder 763

(*Contents continued on page 14*)

In Surgical Sutures

Ligatures

(Armour's)

SURGICAL CATGUT

PHARMACEUTICAL PRODUCTS

SATISFACTION lies in strength, sterility and uniformity of absorption, features to be attained only when the smooth or detached side of selected sheep gut is employed. Right now the price of raw material is very high. Some manufacturers are evening up things by using the mesenteric as well as the smooth portion of the intestine. None of the cardinal qualities can be guaranteed when the rough side is employed. This is obvious to the man who has studied the manufacture of catgut.

In the Armour Laboratory nothing but the smooth, straight side of the gut is put into surgical ligatures. This material is sterilized chemically and thermically at opportune stages and finally the finished suture is, after being placed in tubes, subjected to a degree of heat that means death to all spores and organisms.

The Armour Non-boilable Catgut Ligatures are as flexible as a silk cord, and are of full strength and absolute sterility.

Specify Armour's Non-boilable Catgut Ligatures. You will be satisfied.

PITUITARY LIQUID
(Armour)
the Premier Product of the kind, 1 c. c. ampoules—surgical, ½ c. c. ampoules obstetrical.

SUPRARENALIN SOLUTION 1:1000
Astringent and hemostatic. Stable and non-irritating.

Headquarters for the Endocrines and other Organotherapeutics

ARMOUR AND COMPANY
CHICAGO

For the requirements of

Modern Diagnosis

use "E. S. I. Co."

Electrically Lighted Instruments

The Electro Surgical Instrument Company, the pioneer manufacturer of these instruments, offers the Medical Profession a complete line constructed in accordance with the suggestions and coöperation of the eminent Physicians and Surgeons by whose names the instruments are designated

Nasopharyngoscope—*Holmes.*
Transilluminators—*Sullivan.*
Bronchoscopic Instruments—*Jackson, Lynah.*
Cystoscopes—*Braasch, Young, Kelly, E. S. I. Co.*
Urethroscopes—*Swinburne, Young, Gordon, Koch, MacGowan, Ballenger.*
Rectal Instruments—*Tuttle, Lynch, Axtell, Bassler, Beach, Buie.*

Illuminated Eye Spud, Nasal Snare, Mouth Gag, Vaginal Specula, Rectal Specula.

Auriscopes, Nasal Specula, Tongue Depressors, Laryngoscopes.

Tungsten Batteries.

Socket Current Controllers.

Cautery Transformers.

Electrically Lighted Surgical Instruments

To obtain proper service from our instruments, make certain you are using genuine "E. S. I. Co." lamps. For your convenience in ordering correct lamps, write for a copy of our Lamp Sheet.

The Ninth Edition of our Catalogue

describes and illustrates our complete line of instruments, designed both for the work of the specialist and of the general practitioner. A copy will be mailed upon request.

ELECTRO SURGICAL INSTRUMENT CO.

ROCHESTER, N. Y.

CONTENTS—(*Continued*)

Knock-knee and Bow-leg 763
Endothermy in the Treatment of Accessible Neoplastic Diseases . . . 763
Brain Abscess with Pathological Observations 763
Simple Ulcers of the Jejunum and Ileum 764
Carcinoma of the Papilla of Vater 764
Studies on the Ureter and Bladder (with Especial Reference to Regurgitation of the Vesical Contents) 764

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.

A Clinical Study of Rickets in the Breast-fed Infant 765
A Study of Three Hundred Cases of Pertussis in a Hospital 766
Acute Infections of the Urinary Tract—Pyelitis 767

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.

The Wassermann Reaction in Diabetes 768
The Roentgenotherapy of Pointed Condyloma 768
Syphilis in the Bechuana and Native 768

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D., AND FRANK B. BLOCK, M.D.

Treatment of Acute Salpingitis 769
Results of Treatment of Bladder Tumors 771
An Antiseptic Pyelographic Medium 772
Microscopical Compared with Clinical Diagnosis of Uterine Cancer . . 773

(*Contents continued on page 16*)

In HAYFEVER

AFENIL IS INJECTED INTRAVENOUSLY FOR THE PREVENTION and TREATMENT of HAYFEVER

A STANDARDIZED
ORGANIC CALCIUM COMPOUND
IN AMPULES

Afenil

For sale by
MERCK & CO.
NEW YORK, ST. LOUIS, MONTREAL

Literature from
E. BILHUBER, INC.
25 WEST BROADWAY, NEW YORK

Grass Hay Fever

THE Late Spring and Early Summer Type of Hay Fever is occasioned chiefly by grasses. To assure the advantage of preseasonal treatment early diagnostic tests should be made with Timothy, Bermuda Grass, Johnson Grass, etc., according to locality. List of Grasses showing regional distribution and time of pollination sent on request.

TIMOTHY *Phleum pratense*

BERMUDA GRASS *Cynodon dactylon*

JOHNSON GRASS *Sorghum halapense*

The Arlington Chemical Company

Yonkers, New York

Ideal Hay Fever Treatment

The 15-dose series of Mulford Pollen Extracts in ever-ready Hypo-Units

MULFORD HAY FEVER POLLEN EXTRACTS are the specific pollen proteins in refined form, accurately standardized in terms of protein units.

THE MULFORD HYPO-UNIT package is the last word in convenience, safety and accuracy. Each Hypo-Unit contains one accurately measured dose, and is sterile and completely assembled, ready for instant use.

Free Cutaneous Tests and literature sent to physicians on request

60111

H. K. MULFORD COMPANY, PHILADELPHIA, U. S. A.

Mulford

THE PIONEER BIOLOGICAL LABORATORIES

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M., AND DE WAYNE G. RICHEY, B.S., M.D.

The Influence of the Suprarenal Cortex on the Gonads of Rabbits . . 774
Diphtheritic Vaginitis in Children 774
Immunological Significance of Vitamins. Influence of the Lack of Vitamins on the Production of Specific Agglutinins, Precipitins, Hemolysins and Bacteriolysins in the Rat, Rabbit and Pigeon 775
Influence of Lack of Vitamins on Resistance of Rat, Rabbit and Pigeon to Bacterial Infection 775
Influence of the Lack of Vitamins on the Leukocytes and on Phagocytes 776
Chloride Retention in Experimental Hydronephrosis 776

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.

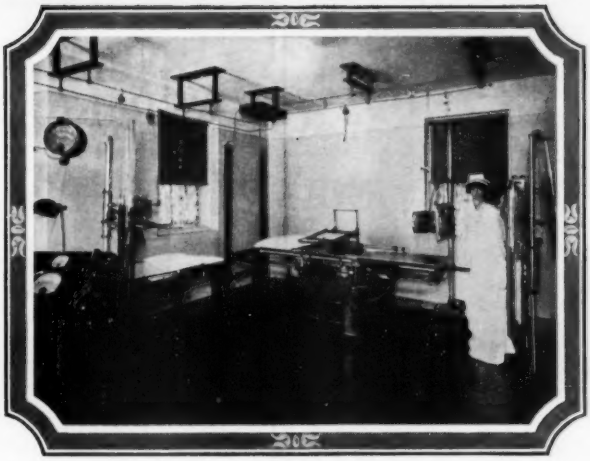
Recurrent Serum Rashes 777
An Epidemiological Study of Folliculosis of the Conjunctiva 778
Diphtheric Vaginitis in Children 779
The Elimination of Carbon Monoxide from Blood by Treatment with Air, with Oxygen, and with a Mixture of Carbon Dioxide and Oxygen . 779
Efficacy of Botulinus Antitoxin 780

Digitan

is physiologically standardized. It insures uniform digitalis effect.

Powder *Tincture*
Tablets *Ampuls*

MERCK & CO.



A Service Which Strives for the Perfection of Roentgenology

". . . a spirit of helpfulness that the radiographer appreciates."—Dr. Brooksher, Chicago.

"His work . . . was so perfect and satisfactory . . . that we cannot help but express our appreciation."—St. Mary's Hospital, Pueblo, Col.

"He . . . rendered us a great deal of assistance and gave us just the information we wanted."—Gunby, Hoard, McElhannon, Wolfe and Gunby, Dallas, Texas.

"We appreciate your men and their service."—Dr. Henry A. Johnson, Tekamah, Nebraska.

"The service included in our contract has been found to be most valuable."—Kootenay Lake General Hospital, Nelson, B. C.

Victor Service begins in Victor Research, includes the manufacturing of Victor X-Ray equipment according to the highest standards, and ends only when the practitioner or hospital is thoroughly satisfied.

Victor Service works for an ideal—the perfection of roentgenology in all its phases.

Hence the Victor Service Stations do much more than send out men to make repairs. It is one of their functions to keep the physician abreast of the improvements made in X-Ray apparatus and consequently in technique.

Every Victor representative is a *factory-trained* man, and is therefore competent to advise intelligently with you in the selection, installation and operation of X-Ray equipment.

VICTOR X-RAY CORPORATION, 236 South Robey St., Chicago, Illinois

Sales Offices and Service Stations in All Principal Cities

VICTOR

Is there Curative Value in Radio-active Waters?

An analysis of the springs at Hot Springs, Virginia, to determine the radio-activity of the water was made in 1913 by Professors Ernest Zubelin and J. C. Hemmeter. They reported a very high degree. A very favorable comparison with the greatest European spas.

When these facts were published—a great cry went up from the medical world. They questioned the value of radio-action in water. The value of water as a therapeutic agent has always been approved of. The new problem was—is there an especial curative value in radio-active waters?

Radium is hailed as the biggest discovery of the times in curing certain diseases. This was the basis of belief that spas rich in radium emanation would also prove of great curative benefit. Many tests were made at the European spas. Very favorable results were reported. At the Radium Institute in London the same tests were tried out. There, too, successful cures were made—especially in cases with gouty manifestations.

Can we take these successful cures as an indication that the presence of radio-action in water is highly curative?

We believe so. Especially because in our own thermal establishment, we have brought relief and cure to so many persons.

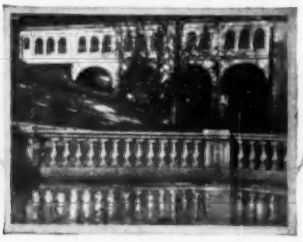
Literature specially prepared for physicians will be sent on request

Virginia Hot Springs

The HOMESTEAD

Christian S. Andersen, Res. Mgr.

Hot Springs - Virginia



NEUTRAL ACRIFLAVINE

—*"Its powerful antiseptic potency has been demonstrated by most careful tests"*

DOCTORS, surgeons, medical men in all fields of the profession have tried Neutral Acriflavine (National) and endorsed it—enthusiastically.

They are using it on burns—in ear and mouth infections—in treating gonorrhea—for intravenous application—*for all cases that require an antiseptic of unusual strength*!

Let us send you the Medical Booklet that outlines the importance of Neutral Acriflavine. It gives you actual reports of specific results achieved by doctors and surgeons in all fields.

Pharmaceutical Division

National Aniline & Chemical Company, Inc.

40 Rector Street, New York, N. Y.

Neutral Acriflavine

"NATIONAL"

—one of the National Medicinal Products

The original American Neutral Acriflavine
Passed by the Council on Pharmacy and Chemistry

Pharmaceutical Division
National Aniline & Chemical Company, Inc.
40 Rector Street, New York

Please send me your booklet on "Neutral Acriflavine and Acriflavine," containing complete bibliography, clinical reports, etc.

Name.....

Professional Address.....

Three Leading S. & G. Products With Substantial Claims to the Distinction Of Favorites in Your Armamentarium

Atophan

TRADE MARK

Reg. U. S. Pat. Off.

Since 1911 the foremost remedy for the relief and treatment of Rheumatic, Gouty, Neuralgic, Neuritic and Sciatic Conditions.

Furnished in
Tablets, 7½ grains, 20 in box
Powder, 1 ounce cartons.

A Non-Narcotic Synthetic with highly potentiated Analgesic and Sedative Action. Especially indicated in "Headaches" of the nervous, menstrual and habitual types; in sleeplessness due to Pain and in Drug Withdrawal Cures.

Furnished in
Tablets, 3 grains, 12 in tin and 100 in bottle
Powder, ¼ oz. and 1 oz. bottles.

TRADE MARK

PERALGA

Reg. U. S. Pat. Off.

Anusol
HEMORRHOIDAL
Suppositories

Reg. U. S. Pat. Off.

Prescribed and recommended for over a quarter of a century by physicians everywhere for the Non-Surgical Treatment of Hemorrhoids and other inflammatory Rectal Disorders.

Furnished in boxes of 12 Suppositories.

Information and Complimentary Trial Quantity to make you acquainted, if still necessary, or to refresh your memory—lest you forget

SCHERING & GLATZ, INC.

150-152 Maiden Lane
NEW YORK

Manufacturing Laboratories
BLOOMFIELD, N. J.

THE INTRAVENOUS USE

of

MERCUROCHROME—220 SOLUBLE

as reported by

HUGH H. YOUNG, M.D., and JUSTINA H. HILL, M.S.
"The Journal," A. M. A., March 1, 1924

"These cases (see case reports in reference) are sufficiently varied to show a wide field of usefulness for Mercurochrome—220 soluble as an intravenous germicide; but just what the limitations of its use may be will have to be determined by a much more extensive series of trials. That certain localized infections may now be safely subjected to the experimental use of intravenous therapy is shown by some of these cases, and there can be no doubt that when blood cultures show a generalized septicemia, mercurochrome and gentian violet can be offered with the hope of preventing an otherwise surely fatal ending."

A comprehensive circular on the general uses of Mercurochrome and a leaflet on its intravenous administration will be furnished on request

HYNSON, WESTCOTT & DUNNING, Baltimore, Md.

POLLEN ANTIGENS
Lederle

FOR PROPHYLAXIS OF

HAY FEVER

Pollen Antigens *Lederle* have been prepared continuously over a period of ten consecutive years by our original method of extracting the mature dried Pollen in 66⅔% glycerol and 33⅓% saturated sodium chloride solution.

Pollen Antigens *Lederle* have yielded uniformly favorable results during this period.

Pollen Antigens *Lederle* are standardized serologically by the complement-fixation method which insures their antigenic activity.

Pollen Antigens *Lederle* will not deteriorate.

Further information and illustrated treatise on request

Diagnostic tests to physicians without charge

The name Pollen Antigen denotes the product of the LEDERLE ANTITOXIN LABORATORIES

LEDERLE ANTITOXIN LABORATORIES
511 FIFTH AVENUE, NEW YORK CITY

NOTE:—Send us this advertisement with your name and address on the margin and we will send full information

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

MAY, 1924

ORIGINAL ARTICLES.

EXPERIMENTAL STUDIES IN ELECTROIONIC MEDICATION.

By George T. Pack, M.D., Frank P. Underhill, Ph.D.,

and

Joseph Epstein, M.D., and I. Newton Kugelmass, Ph.D.,

new haven, conn.

(From the Department of Pharmacology and Toxicology, Yale University, New Haven, Conn.)

Introduction. The so-called electrolytic absorption of drugs has fascinated the medical physicists for more than a century. At the present time this method is quite in vogue in England and France, but has suffered neglect in America, except in the dental profession. Most of the current literature, peculiar to this field of medication, is distinctly clinical in origin; the favorable results have almost invariably been attributed to the pharmacological behavior of the introduced drug, with little consideration of the physiological effects of the electrical current *per se*. Bearing in mind the ancient aphorism, "Nature tends to effect a spontaneous cure," we decided that a goodly portion of the accumulated data to date had not been collected under control conditions so satisfactory as to warrant such sweeping laudations upon this method of administration of drugs. Consequently, a series of laboratory experiments were performed, some of which are original; others are repetitions under the standardization of controls, thus confirming and contradicting previously published results.

The Electrochemical and Electrophysical Basis. A brief résumé of electrochemical phenomena associated with this method is

necessary in order to comprehend the changes which occur within the body subsequent to the introduction of drugs through the skin by means of the electric current.

The galvanic or continuous current is applied to the phenomena which occur throughout the length of a conductor, the two ends of which are maintained at different potentials by an electromotive force. The typical continuous current is that obtained from an ordinary galvanic cell consisting of two metals immersed in a conducting liquid. If we connect the free ends of the two metals (the so-called poles or electrodes) a continuous electric current is produced. If we insert the human body (a conducting medium) in the circuit then the current will flow in the same direction. The point of entrance of the current is the anode or positive pole and the point of exit, the cathode or negative pole (Fig. 1).

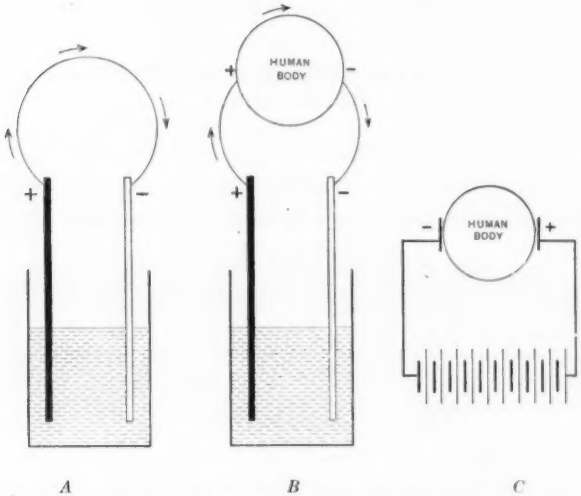


FIG. 1.—*A*, the galvanic cell (the arrow indicates the current course); *B*, the human body in the current circuit of a galvanic cell; *C*, the human body in a galvanic battery circuit.

Conducting media of the electric current are aqueous solutions of acids, bases and salts. Arrhenius demonstrated that these substances (electrolytes) are dissociated or split in water into their constituent atoms or groups of atoms called ions, which carry a positive charge or negative charge of electricity. Each molecule of the electrolyte furnishes two kinds of ions with equal and opposite charges of electricity.

The current remains constant so long as the potential at the extremities of the conducting medium remains constant and may be graphically portrayed (Fig. 2).

3104 c 1
19 Jy 44

The current loses in strength because of resisting forces opposing it. The strength of the current that is actually effective in the animal body, therefore, will increase with the number of galvanic

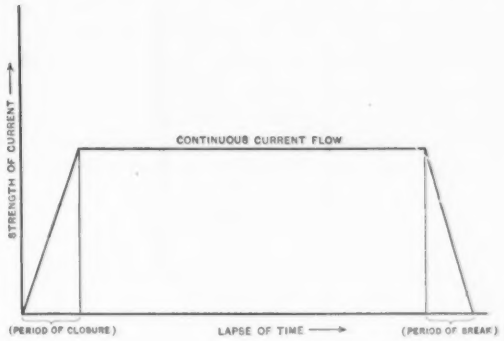


FIG. 2

cells, and will decrease with the resistance offered, and *vice versa*. Ohm's law formulates this as:

$$\text{Current strength (amperes)} = \frac{\text{Electromotive force (volts)}}{\text{Resistance (ohms)}}.$$

The body resistance is variable and among the tissues the skin's resistance is greatest. The resistance of the skin is less when moistened, especially over sweat-gland ducts or hair follicles, as shown by the use of colored ions, the glandular orifices being the site of the colored deposit. The order of resistance of animal tissues is bone > fat > tendon > skin > muscle > blood > nerve.[1] The smaller the surface of the electrode in contact with the skin the more the lines of electric flux are concentrated in passing through the tissue immediately subadjacent to the electrode (Fig. 3).

Considering the body tissues as aqueous ionic solutions, the physicochemical effects of the electrical current upon solutions of electrolytes are:

1. Orientation of ions.
2. Penetration of ions.
3. Electrolysis.

1. *Orientation of Ions.* Solutions of electrolytes contain ions and molecules all in dynamic equilibrium among themselves and in constant motion. With the passage of a current through such a solution, a rearrangement of the ions results at once: The positively charged ions (cations) are repelled from the positive and attracted by the negative pole (cathode); the negatively charged ions (anions) are repelled from the negative and attracted to the positive pole (anode). "Likes repel and unlikes attract." The

effect then is simply directive, and this migration of the ions represents to us that which we call an electric current in an electrolyte.

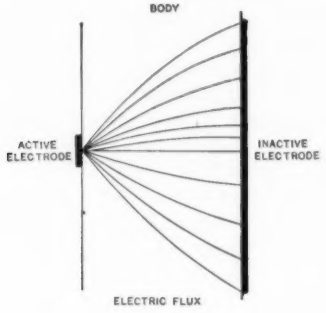


FIG. 3

2. *Penetration of Ions.* We are indebted to Hittorf for the discovery that there is a wide variation in the velocity with which the various ions migrate through the electrolyte, *e. g.*, the hydrogen ion moves about five times as fast as the chlorine ion. Knowing that the electric current is transmitted through the electrolyte wholly by the charges carried by the moving ions, Kohlrausch, by quantitatively estimating these electric charges per unit of time, was able to deduce the velocity of the ions themselves in aqueous solution. This fact has therapeutic import, as we shall see later.

THE PENETRATION OF SALTS.

Anode.	*Body.*	*Cathode.*
M^+ M^+	Na^+ Na^+ Na^+ Na^+	M^+ M^+
R^- R^-	Cl^- Cl^- Cl^- Cl^-	R^- R^-

BEFORE THE PASSAGE OF CURRENT.

Anode.	*Body.*	*Cathode.*
M^+	M^+ Na^+ Na^+ Na^+	Na^+ M^+ M^+
R^- R^- Cl^-	Cl^- Cl^- Cl^- R^-	R^-

AFTER THE PASSAGE OF CURRENT.

Although the quantity of the substances separating at the electrodes is proportional to the quantity of the current, the migrational velocity of the ions is independent of this electrical force, according to Hittorf. (Many of these ions are lost, only a portion of them migrating or transferring; the quantity of cations and anions of this latter number, however, has an equal ratio to that of the migrational velocity of cations and anions.) Hittorf, moreover, found that the concentration of the solution is the all-important factor. We are cognizant of this fact—that the greater the

degree of dissociation of the solute, the greater the facility with which the current travels, since the conductance of a solution is due to the dissociated parts of the molecules.[2] Hittorf further found that the large number of undissociated molecules in the concentrated solution offered a considerable degree of resistance to the motion of the ions among them. This resistance may be overcome by increasing the dilution (and consequently the degree of dissociation) until a certain point is reached where dissociation is complete and the maximal value of electrical conductance is obtained. This serves to demonstrate to us the fallacy in the use of concentrated solutions of drugs at the electrodes.

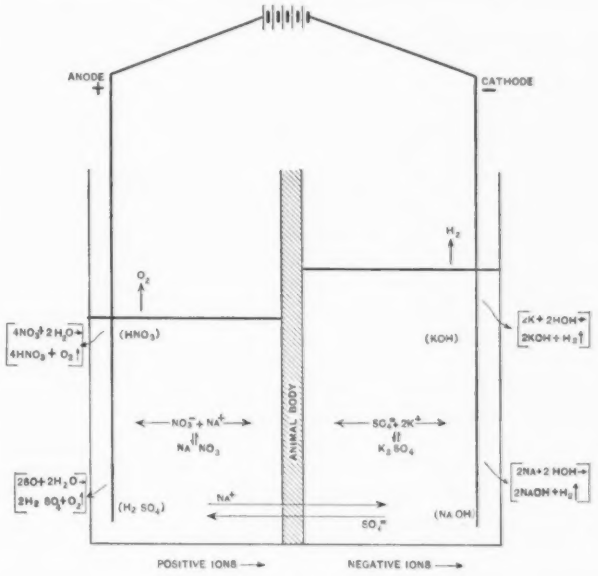
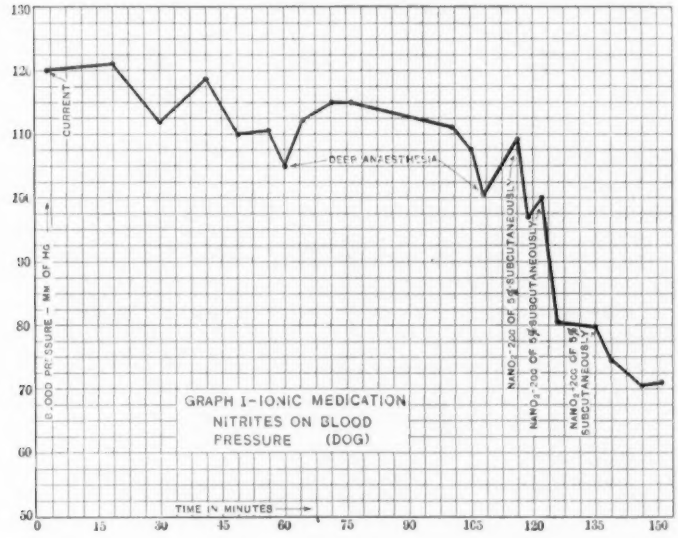


FIG. 4

We may state then that the percentage of the solution used is unimportant (provided it is dilute enough), since the quantity of ions introduced into and through the skin is more or less proportional to their chemical equivalents.[3] Quite at variance with the velocity of the ions, the number of migrating ions is dependent on the quantity of current—the milliampèrage—since more ions are necessary to transport the electrical charges. The migrational velocity is important, nevertheless, in the passage of the current, since the quicker moving ions convey the greater part of the current, *e. g.*, hydrogen ions carry five times the quantity of electricity that is carried by chlorine ions.

3. *Electrolysis.* Permit one arm of the body to be immersed in a solution of $NaNO_3$ at the positive pole, with the other arm in a K_2SO_4 solution at the negative pole. The attraction and repulsion of anions and cations by anode and cathode may then be graphically portrayed (Fig. 4). The Na and SO_4 ions are the migratory ions within the body. When these ions reach the electrodes of their respective destinations (assuming that the body is a permeable and conducting medium) they give up their charges and consequently are released in the electrically neutral state. Having lost their charges, they unite with water forming NaOH around the negative pole and H_2SO_4 at the positive pole. These changes are indirectly the secondary effects of the electric current (Fig. 4).



Since platinum is an inactive electrode, these chemical changes at the poles are devoid of particular significance, providing platinum is utilized, although in time a polarization and a consequent antagonistic polarization current may develop. However, if the electrode is a soluble one it will react chemically with the acid or base and consequently may interfere with the success of the experiment. In some instances the electrode is intentionally composed of the same metal as the cations of the medicament to be introduced, in which case the continuous solution of the electrode by newly formed acid occurs. This is desirable, since it augments the supply of these particular ions within the solution; for example, a positive zinc electrode in a solution of zinc sulphate.

To use other than an inactive electrode, except in the above instance, complicates the study of this method of introducing drugs. Metals higher in the electromotive-force series displace inferiorly placed metals from their salts; thus, a zinc electrode in a solution of mercuric nitrate deposits mercury and forms zinc nitrate, which then assumes the role of electrolyte.

Experimental Procedure. The electrodes are applied to the human body by one of two methods. The arms or legs may be immersed in separate solutions, which in turn are in contact with the electrodes. One solution contains the medicament to be introduced through the skin, the other solution being 1 per cent NaCl. The positive or negative electrode is utilized according to whether the desired ion is cation or anion.

The other method is the employment of thick layers of lint, saturated with the solution, between the skin and electrode. The introducing pole is placed over that area of skin, through which the drug desires ingress. The opposite pole may be placed anywhere on the body. We have mentioned the concentration of acid and alkali forming at anode and cathode. To circumvent the deleterious action of these caustics upon the skin, very thick layers of lint must be employed, or a porous cup may intervene between electrode and lint (Inchley).[4] The lint must be applied smoothly, contact being even, otherwise a burn may result.[5] An instance of this may be cited in Rolfe's careful adaptation of sheet-zinc electrodes to fit in the folds of the nates during the treatment of pruritus ani.[6]

The quantity of current comfortably tolerated by the patient is 2 or 3 ma. (Fowler[7] used 20 to 30 ma. for one-half hour.) A greater milliampèrage provokes decidedly unpleasant sensations of burning, pricking and throbbing. The larger the electrodes, the less discomfort attends the passage of the current. Some therapeutists advise using a current of 2 or 3 ma. per 1 sq. cm. of electrode surface.[8] The quantitative factor in this mode of drug administration is not only the strength of current, but also the duration of its passage. The product of the number of milliampères per 1 sq. cm. of electrode contact, by the time of the passage of the current, gives a figure which is approximately proportional to the number of ions introduced,[8] *e. g.*, 1 ma. for thirty minutes is equivalent to 2 ma. for fifteen minutes.

What voltage is necessary for the success of this procedure? If we recall Ohm's law we may then realize that the voltage employed depends upon the resistance of the individual. The human body is remarkably resistant to the passage of the electric current. Voltages of 60 to 110 have been used by other investigators, but 20 to 30 volts have proven ample in our experiments on lower mammalia. The electrodes, of course, are in apposition with the skin before the current is turned on, the milliampèrage and voltage

being gradually increased from zero to the desired amount and as slowly decreased at the completion of the treatment. This prevents shock and permits the tolerance of a stronger current.

The drug should be dissolved in the preparation to make a 1 per cent solution.

In the human experiments the immersion method only was used. With dogs as the experimental animals, the topical applications of lint upon abdomen and chest were employed.

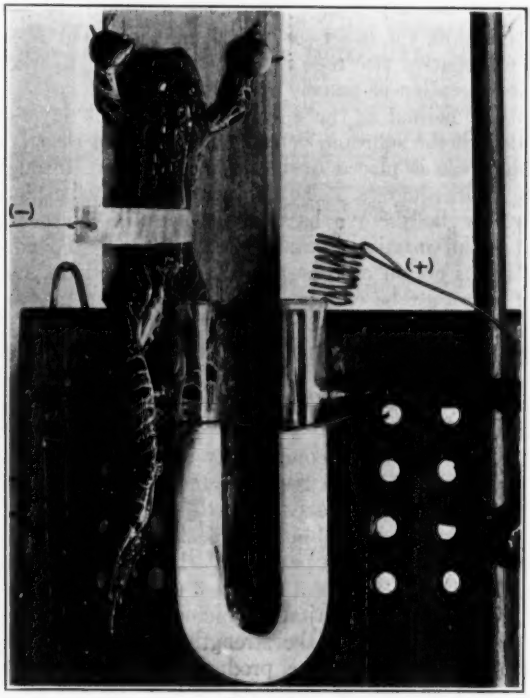


PLATE I

Plate I demonstrates how frogs were arranged. The live frog is suspended, one leg dipping into one arm of a U-tube, which contains the solution of the drug. The other arm of the U-tube holds platinum electrode. The opposite pole is a metal band upon lint surrounding the abdomen. The rheophores may be seen leading to the source of the current. Symptomatology was the only criterion of the success of this measure. We realize that the skin of the frog is not comparable to human dermis, because it is more permeable, and in addition has under it numerous lymph sacs which facilitate systemic absorption. Nevertheless, the relative rapidity

of absorption with and without the electric current is instructive and conclusive.

The mode of procedure with the rabbit: The unnarcotized animal is placed upon a rabbit board. The dependent ears are placed within two beakers. One beaker contains a solution of the drug, the other a 1 per cent solution of NaCl. Platinum electrodes immersed in the solutions connect with rheophores to the source of the current.

The methods of procedure may be tabulated as follows:*

1. The influence of the electric current upon the absorption of metals.
2. The influence of the electric current upon the absorption of alkaloids and glucosides.
3. The influence of the electric current upon the absorption of halogens, non-metals and acids.
4. Detoxication of the body by means of the electric current.
5. The treatment of experimental infections by electrolysis.

The Influence of the Electric Current upon the Absorption of Metals.

MERCURY. Because of the many disadvantages attending the administration of mercury in the treatment of syphilis, we deemed it opportune to test the efficiency of this method. Dogs and rabbits were the experimental animals. A typical protocol is submitted.

EXPERIMENT VI.—Rabbit II; weight, 1.4 kg.

Purpose. Introduction of mercury into the body by the electric current.

Conditions. Voltage, 20; milliampèrage, 7; electrodes, platinum; time, two hours daily for three days.

Methods. The rabbit ears were immersed in two beakers containing respectively NaCl (1 per cent) and $Hg(NO_3)_2$ (3.2 gm. per 100 cc) M/10. The negative pole was inserted in the former solution, and the positive pole in the latter.

Remarks. After five minutes small corroded areas began to form on the positive ear. They were seen to commence in a form resembling small red blisters about 2 mm. in diameter, with a white mucoid-like pin-point area in the center. Many of these coagulated blisters later became confluent. These lesions may be attributed to phenomena induced by the passage of the current, inasmuch as similar lesions by current and control immersions were not provocative of any disturbances.

Symptoms. Symptoms indicative of mercurial poisoning(nephritis, stomatitis, diarrhea) did not appear. Daily urine analyses over the period of a week did not detect mercury by such methods

* In every case the experiment was carefully controlled by noting: (*a*) The influence of the electrical current *per se*, and (*b*) the effect of similar applications of the drug without the aid of the electrical current. Any experiment cited is merely an illustrative example of a series of confirming experiments.

as the Reinsch, potassium-iodide and zinc-amalgamation tests. Feces were likewise negative.

Similar negative results were found in 2 dogs and 5 other rabbits. The explanation is, no doubt, the same as Turrell's excellent reasoning for the non-absorption of zinc:[9] "The zinc ion attracted from the positive electrode to the negative pole, on arriving at the surface of the body, lags behind, and the current is carried on much faster by the H ions of the tissues. The zinc ion is thus free to enter into chemical combination with the tissue constituents and forms an oxychloride of zinc, which is electrically deposited upon the superficial tissues. The process is one of electrodeposition, resembling electroplating of commerce. . . . The skin or mucous membrane thus forms a 'virtual' negative pole." This is exactly what happens in the experiments with mercury. As long as the mercuric ions are electrically charged they do not chemically unite, but as soon as they lose their charge they form mercuric proteinate with the tissues. This coagulation occurs quite superficially, but in time is redissolved in the body fluids. Turrell[10] quotes Sir Oliver Lodge as saying: "The procession of ions continues until it meets with some discontinuity—either some change of liquid or some solid conductor. At a change of liquid, another set of atoms continues the convection." He further cites Chatsky's experiment, as confirming the theory that when a change of liquid occurs in the interpolar path there is a transferal of electrical charges by the ions. It is our belief that this obstacle occurs quite frequently, due to such things as the superficial circulation in the skin, lymph currents, etc.

Cross,[5] by an experiment *in vitro*, concludes that the slow migration of the lead ion is due to its precipitation with salts of the tissue. He simulates the colloidal-tissue fluids by using a solution of gelatin in tap-water. We must agree that the body is a complex electrolyte.

We believe also that the relief experienced in the stiff joints of rheumatoid arthritis by the ionization treatment with the mercuric ion of mercuric succinimide (Clark) is due to the electric current itself, and not to the introduction of the mercuric ions.

Zinc. Although we did not use zinc in our experimentations, yet it is considered here because it proves that the heavy metals are efficient only for local therapy and not for systemic administration, *i. e.*, by the electroionic method. Dilute solutions of $ZnCl_2$ or $ZnSO_4$ applied at the positive pole have been reported by Friel[11] as beneficial or curative in the following conditions: Empyema of maxillary, frontal and sphenoidal sinuses, impetigo of face, eczema, ulcers of arms and legs, chronic otorrhea.[12] Rolfe[6] uses zinc ionization in the treatment of pruritus ani, while Clark[8] enumerates a host of localized lesions for which zinc therapy has been employed.

TREATMENT OF TUMORS. Borrel *et al*[13] treated implanted sarcoma in rats by fixing positive carbon electrodes on compresses saturated with various metallic solutions over the tumor. Curative results were obtained in a number of instances, especially by the lead ion. Disappearance of a cancer of the rectum has been reported, by Wardle,[14] subsequent to zinc ionization, using a current of 60 ma. for thirty minutes on alternate days. Clark removes multiple warts by magnesium ionization. It is agreed that the metals deposited on the surface of the tumor are somewhat corrosive, but the destructive action is probably not due to this alone. Referring to the above protocol, it is noted that even a milliampèrage of 7 produces coagulative phenomena. A milliampèrage of 60 would be quickly destructive. Liquefaction occurs at the negative pole; coagulation at the positive. This latter phenomenon is utilized in the coagulation of blood in aneurysmal sacs by electrolysis. All of these facts lead us to believe that the good results obtained in the treatment of tumors, and the various local lesions mentioned, are due in large part to the action of the electric current *per se*.

MAGNESIUM (CALCIUM ANTAGONISM). Magnesium anesthesia cannot be induced in the rabbit by ionic medication. Success was obtained with frogs as the experimental animals. Control immersions were unproductive of any symptoms.

EXPERIMENT XXV.—Frogs.

Purpose. (*a*) To induce anesthesia by the introduction of magnesium into the body by the electric current; (*b*) to antagonize magnesium action by calcium similarly exhibited.

Conditions. Voltage, 10; milliampèrage, 0.5; electrodes, platinum. Time: Part *a*, six minutes; Part *b*, seven minutes.

Methods. The frog was placed within the circuit, after the arrangement illustrated in Plate I. $MgSO_4$ (5 per cent) was placed within the U-tube at the positive pole. Later $CaCl_2$ (5 per cent) replaced the magnesium sulphate solution.

Symptoms. One and a half minutes after the initiation of the current flow, the respiration became quite rapid, subsiding quickly to extremely slow ones. Flaccidity was noted at the two-minute interval. At six and a half minutes the frog was entirely flaccid. The animal was narcotized and anesthetized, as judged from the response to stimulation. Pupils were contracted to the degree of narcosis. At this point the $MgSO_4$ was removed and the $CaCl_2$ substituted. One-half minute later the pupils began to increase in size. The animal again responded to stimulation. Recovery had evidently occurred. However, seven minutes subsequent to the calcium substitution, the frog became quite stiff. The pupils were again contracted. Examination revealed that this condition was not a true spasticity, but a rigor, which probably accounts for the terminal pupillary and skeletal muscle changes.

Remarks. The systemic symptoms are attributed to lymphatic absorption, subsequent to the introduction of these metals through the skin. The Mg–Ca antagonism was earlier discovered by Meltzer.

BARIUM. Experiments with barium chloride were negative, although conducted in a manner identical with the above. The end-point desired was the death of the animals with the ventricles in systole and the auricles in diastole.

The Influence of the Electric Current upon the Absorption of Alkaloids — Neutral Principles, Etc. STRYCHNIN. Stephen Leduc, the father of electroionic therapy, first produced strychnin convulsions in a rabbit by "driving" in the strychnin ion by means of the galvanic current. Inchley[4] has recently confirmed this, but has modified Leduc's theory by stating that strychnin is fatal because it is carried by the blood stream from the superficial tissues to the spinal cord. A protocol of one of our typical experiments is as follows:

EXPERIMENT XXI.—Rabbit; weight, 1.8 kg.

Purpose. To introduce strychnin into the body by the electric current.

Conditions. Voltage, 20; milliampèrage, 12.5; time, 6.38 to 7.40 P.M. (sixty-two minutes).

Procedure. Ears of rabbit were immersed in beakers; positive pole, beaker of 2 per cent strychnin sulphate; negative pole, beaker of 1 per cent sodium chloride.

Observations. 7.00: Definite general hypersensitiveness to touch; reflexes very acute; twitches to stimulation; marked defecation.

7.40: Sudden opisthotonic convulsion with cessation of respiration.

7.45: Rabbit removed from board; body is stiff and arched; this gradually was replaced by tremors and finally flaccidity; another convulsion followed, during which death occurred at 8.00 P.M.

Remarks. Control experiments of (*a*) immersion and (*b*) current alone were negative.

EXPERIMENT XXIV.—Frog.

Purpose. Strychnin introduction, as above.

Conditions. Voltage, 20; milliampèrage, $\frac{1}{2}$.

Procedure. (Plate I.) Two per cent strychnin sulphate at positive pole in U-tube.

Observations. 10.38 to 10.40: Current on.

10.40: Current off; leg washed thoroughly.

10.50: Hypersensitiveness.

11.00: Typical convulsions.

Control. No current used; leg immersed as above.

10.59 to 11.01: Leg immersed in 2 per cent strychnin sulphate.

11.01: Leg washed thoroughly.
11.35: Slight hypersensitiveness.
11.55: More hypersensitive.
12.45: Typical convulsions.
Remarks. The difference in the rapidity of the onset of convulsions may be attributed to the influence of the electric current.

PICROTOXIN. EXPERIMENT XXXII.—Frogs.
Purpose. Picrotoxin introduction through the skin by the electric current.
Conditions. Voltage, 20; milliampèrage, $\frac{1}{2}$.
Procedure. (Plate I.) Two-fifths per cent picrotoxin at positive pole in U-tube.
Observations. 4.29 to 4.35: Current on.
4.32: Hypersensitive.
4.35: Current off; typical convulsions; picrotoxin croak, etc.
Control. 4.40 to 5.10: Leg immersed in 0.4 per cent picrotoxin; no current.
5.10: Convulsions.
Remarks. The electric current hastens the skin absorption of picrotoxin; picrotoxin is a poor electrolyte.

VERATRIN. EXPERIMENT XII.—Frogs.
Purpose. Veratrin introduction through the skin by electric current.
Conditions. Voltage, 20; milliampèrage, $\frac{1}{2}$.
Procedure. (Plate I.) Two per cent veratrin at positive pole in U-tube.
Observations. 5.29$\frac{3}{4}$ to 5.30: Duration of current and immersion of leg.
5.31: Characteristic veratrinization. Frog is clumsy. Muscles contract well, but do not relax.
Control. 10.35 to 10.36. Leg immersed in 2 per cent veratrin solution.
10.45: Definite signs of veratrin action on skeletal leg muscle.
Remarks. Veratrin is absorbed very quickly by the frog skin, but much more quickly with the aid of the galvanic current.

NICOTIN. Nicotin is absorbable by human skin. It is quite rapidly absorbed from mucous membranes, hence is likewise absorbed with ease by the frog's skin.

EXPERIMENT XXII.—Frogs.
Purpose. The absorption of nicotin through the frog's skin with the aid of the electric current.
Conditions. Voltage, 20; milliampèrage, $\frac{1}{2}$.
Procedure. (Plate I.) One-twenty-fifth per cent nicotin placed at positive pole in U-tube.

Observations. 11.12 to 11.15: Current on and leg immersed.

11.15: Current off; leg rinsed.

11.25: Nicotin convulsions; clonic; independent of sensory stimulation.

Control. 11.28 to 11.31: Leg immersed; no current.

11.31: Leg rinsed.

12.20: Individual muscles are hypersensitive; fine tremors like fibrillations; no convulsions.

Remarks. The electric current facilitates the absorption of nicotin.

CURARE. Rabbits could not be curarized by means of the galvanic current, although a milliampèrage of 12 for one and a half hours was used.

EXPERIMENT XXIII.—Frogs.

Purpose. To introduce curare through the skin by means of the galvanic current. Identification by a duplication of Claude Bernard's classical experiment.

Conditions. Voltage, 20; milliampèrage, $\frac{1}{2}$.

Procedure. (Plate I.) Both sciatic nerves were exposed as high on thigh as possible. One leg was ligated tightly, leaving the nerve excluded from the ligature. The unligated leg was immersed in 0.5 per cent curare at the positive pole.

Observation. 10.00: Immersion and current on.

10.05: Diminished response of unligated leg to sciatic stimulation.

10.07: Definite curarization.

Symptoms. (*a*) Stimulation of sciatic nerve of ligated leg; contraction of gastrocnemius of ligated leg; the ligation prevents the curare from reaching the myoneural junctions *via* the circulation.

(*b*) Stimulation of sciatic nerve of unligated leg; corresponding gastrocnemius does not contract, but muscle of ligated leg weakly responds; this is a reflex through the spinal cord, since the sciatic nerve contains both motor and sensory fibers.

Control. Prepared exactly as above. Leg immersed for nineteen minutes; no action.

PILOCARPIN. EXPERIMENT XXIX.—Rabbit; weight, 1.7 kg.

Purpose. To introduce pilocarpin into the body by means of the galvanic current.

Conditions. Voltage, 20; milliampères, 13; time, 2.55 to 3.40.

Procedure. Rabbit's ears immersed; positive beaker, 0.4 per cent pilocarpin hydrochloride; negative beaker, 1 per cent sodium chloride.

Observations. 2.55: Immersion; current on.

3.20: Definite salivation and epiphora.

3.40: Sialagogue action marked (saliva drips from mouth); epiphora increased; the pupils were not contracted; heart-rate is normal; these latter two findings engender doubt as to whether pilocarpin is actually introduced; however, the accelerated glandular activity is suspicious.

Control. Negative for immersion of ears in pilocarpin solution.

CAFFEIN. EXPERIMENT XXXVI.—Rabbit; weight, 2.1 kg.

Purpose. To produce diuresis by the electrolytic introduction of caffein through the skin.

Conditions. Voltage, 20; milliampèrage, 12½; time, two hours.

Procedure. Controls were first run on the same rabbit; each rabbit was deprived of food and water for ten hours previous to the experiment; the normal two-hourly output averaged from 1 to 3 cc of urine; ears were immersed; positive beaker contained 1 per cent caffein citrate; negative beaker contained 1 per cent sodium chloride; upon removal from the rabbit board, the animal was catheterized every two hours and the volume carefully measured.

Results. Control rabbits and those utilized in the experiment alike secreted an average of 1 to 3 cc of urine every two hours; not enough caffein was introduced to modify the secretory activity of the kidney.

LOCAL ANESTHETICS. These confirm the restriction of value of ionic therapy to local areas.

(*a*) COCAIN. Human subject.

Purpose. To produce local anesthesia by the introduction of cocain into the skin.

Conditions. Voltage, 20; milliampèrage, 2.

Procedure. Immersion method. One finger in beaker containing 1 per cent cocain hydrochloride at positive electrode; another finger in negative beaker containing 1 per cent NaCl.

Observation. 3.17 to 3.27: Current period.

3.27: Finger definitely anesthetized and numb; feels asleep; pain not completely absent over entire area of immersion.

4.30: Skin still numb.

4.50: Skin has regained normal sensitivity.

Controls. (*a*) Immersion in 1 per cent cocain solution without the current gives negative results.

(*b*) The current by itself produces a prickling sensation.

Remarks. This method has been used clinically. The directions call for 3 ma. of current per 1 sq. cm. of surface immersed. Fette[3] states that cocain anesthesia by the electrolytic method lasts four to five hours; the reason for the relative prolongation of local anesthesia by this method over that of hypodermic injection, he attributes to the following facts: Cocain, given hypodermatically, is carried away very quickly by the lymph; in the electrolytic method of absorption all osmotic conditions are dominated, and

the cocain enters the cells instead of bathing them so that "the ions accumulate and remain in static equilibrium as a store supply for gradual elaboration by the protoplasm." We do not find cocain anesthesia prolonged by this method.

(*b*) PROCAIN. Human subject.

Purpose. To produce procain anesthesia by driving in procain into the skin by the galvanic current.

Conditions. Voltage, 20; milliampèrage, 2.

Procedure. Immersion method. One finger in beaker containing 5 per cent procain at positive electrode; another finger in negative beaker containing 1 per cent NaCl.

Observations. 3.38 to 3.48: Current period.

3.50: Definite numbness, but not complete anesthesia for pain.

4.30: Sensations have returned to normal.

(*c*) BUTYN. Human subject.

Purpose. To produce local anesthesia by the electrolytic introduction of butyn into the skin.

Conditions. Voltage, 20; milliampèrage, 2.

Procedure. Same as above, only positive beaker contains 1 per cent butyn.

Observations. 4.01 to 4.11: Current period.

4.12: Finger numb; same degree as with procain.

4.30: All numbness gone.

Remarks. Anesthesia is much shorter than with procain, and very much briefer than with cocain.

(*d*) BENZYLCARBINOL. Human subject.

Purpose. To produce local anesthesia by benzylcarbinol, electrically introduced.

Conditions. Voltage, 20; milliampèrage, 2.

Procedure. Same as above, only positive beaker contains 1.5 per cent benzylcarbinol.

Observations. 4.46 to 4.53: Current period.

4.53: Slight, insignificant, temporary numbness.

(*e*) SALICAIN. Human subject. One per cent solution. This is an extremely poor electrolyte. No action could be noted.

QUININ. The local effects of quinin, introduced into the skin by the electric current, have been reported beneficial in cases of herpes zoster. According to Jacoby,[15] quinin has subsequently been recovered from the urine.

ATROPIN. Although the rabbit is markedly tolerant to atropin, Inchley[4] causes a paralysis of the cardiac vagal endings by the introduction of the atropin ion, with the current localized in the tongue.

ACONITIN. Inchley produced delirium cordis and death in a rabbit, with the introduction of the aconitin ion, by a milliampèrage of 25. B. W. Richardson, in 1859, locally anesthetized skin areas with aconite by utilizing this method.

The Influence of the Electric Current upon the Absorption of Halogens, Non-metals, Acids, Etc. The halogens, non-metals and acid radicals are negative ions or anions and consequently are introduced at the cathodal pole.

CYANIDES. Leduc originally performed this experiment which has been validated recently by Inchley.[4] These phenomena are adumbrated in the following protocol:

EXPERIMENT XIX.—Rabbit; weight, 1.6 kg.

Purpose. To introduce cyanides into the body by the electric current.

Conditions. Voltage, 20; milliampèrage, 12.5.

Procedure. The ears of rabbit were immersed in beakers. Positive pole, beaker of 1 per cent sodium chloride; negative pole, beaker of 5 per cent sodium cyanide.

Observations. 5.50 to 6.25: Immersion and current on.

6.10: Tonic convulsions commence and definite air-hunger appears; the symptoms progress gradually.

6.15: Respiration is quite labored; eyeballs protrude, etc.; respiration became weaker and weaker, until the rate was only 19 per minute; the mouth was open wide and the breath came in gasps; conjunctival reflexes were absent; the animal was almost dead.

6.25: Animal removed from apparatus. Sodium thiosulphate injected subcutaneously. Venesection reveals blood of a cherry-red color.

Remarks. The cyanide ion easily enters at the negative pole. Systemic absorption *via* circulation completes the introduction. Attention is called to the fact that by this method the cyanide ion is only gradually absorbed, so that the sequence of symptoms are well portrayed.

Control. Ears immersed for one hour in solutions of identical character and strength; the electric current was not used; no symptoms developed.

NITRITES. The subcutaneous administration of 1 grain of sodium nitrite is sufficient to produce a fall in blood-pressure of 10 to 12 mm. of mercury. That the characteristic vasodilation does not follow the electrolytic method of absorption, is apparent in Graph I. The nitrite ions may form a quite stable chemical union with the superficial tissues, and, in addition, the quantity or concentration of these nitrite ions absorbed by the circulation may be insufficient at any one time to provoke a noticeable pharmacological effect.

EXPERIMENT LX.—Dog; weight, 7.6 kg.

Purpose. To produce vasodilation and a consequent fall in blood-pressure by the electrolytic absorption of the nitrite ions.

Conditions. Voltage, 20; milliampèrage, 15; time, 4.05 to 5.55.

Procedure. The topical application method was utilized. Sodium nitrite (5 per cent) solution saturated the lint pad at the negative pole, which was a platinum plate 3 by 4 inches; at the positive pole was sodium chloride (1 per cent) solution. Mercury manometric readings of the carotid blood-pressure were taken. The depth of ether anesthesia was carefully regulated.

Observations. (See Graph I on page 630.)

Control. The dog was susceptible to nitrite influence as revealed by the terminal hypodermic injection.

SALICYLATES. Clark[3] tabulates the pathological conditions, for the treatment of which a 1 per cent solution of sodium salicylate is used at the negative pole: Myositis, lumbago, sciatica, trigeminal neuralgia, chronic rheumatism and gout. Each rheumatic joint is treated locally, so that, theoretically, beneficial results are not dependent on the presence of the salicyl ion in the general tissues. Inchley,[4] employing a current of 25 milliampères, through an electrode of 20 sq. cm., was not able to introduce the salicyl ion deeper into the joint than occurred with the hypodermic administration of sodium salicylate. The depth of penetration was ascertained by staining the excised tissue with ferric chloride. Insomuch as the deeper-joint structures were unstained, we might infer that this is fallacious therapy. Cross[5] attributes the benefits from salicylate ionization as due to "drastic tissue disturbances, rather than the chemical effects of the specific ion, *e. g.*, in sciatica 15 ma. are necessary to insure relief."

Inchley was able to recover 0.8 mg. of salicylate in the urine at the completion of the first thirty minutes of the above quoted experiment. Evidently a certain amount of circulatory absorption occurs. We, like Maute, were unable to confirm these urinary findings.

The following experiment was planned with the purpose of demonstrating whether sufficient salicyl ions can be introduced to produce systemic effects.

EXPERIMENT XXXVIII.—Rabbit; weight, 2 kg.

Purpose. To test the antipyretic power of the salicyl ion, introduced by electrolytic absorption from the skin.

Conditions. Voltage, 20; milliampèrage, 12.5; time, 11.00 A.M. to 1.00 P.M.

Procedure. Albumose fever was attempted by hypodermic injections of Witte peptone. This was not so productive of pyrexia as were bacterial emulsions of Bacillus coli, given intraperitoneally. The temperatures in our series of 3 rabbits rose to approximately 41° C. (rectal) from a normal temperature of about 38.5°. The rabbit was placed on animal board. Ears immersed. Positive beaker contained 1 per cent sodium chloride; negative beaker contained 1 per cent sodium salicylate.

Controls. The drop in temperature at first was considered specific. However, the same occurred by using sodium chloride solution at both poles. A control, with the rabbit in position on the board only, and no electric current, causes us to believe that the fall in temperature is due to the vascular changes induced by the rabbits' position on the board.

Analysis. Urinalysis is negative for salicylates.

IODIDES. Theodore Clemens, in 1858, was the first physician to advocate the clinical use of the electrolytic transmission of iodin. His purpose was to further the lysis of syphilitic scleroses. A few of the pathological conditions for which the electroionic application of iodin has been reported efficacious are: Localized syphilitic infections, lead palsy, labyrinthian deafness, small skin and mucous membrane tumors,[15] certain iodin-deficient goiters,[8] cicatrices, keloids[16] and pruritus ani.[6]

Iodin has been detected in the urine subsequent to its electrolytic introduction. Bourguignon, by experiments upon himself, quantitated the daily urinary excretion of iodin. By employing 10-ma. current for three minutes daily he was able to recover 6.4 mg. of iodin in the twenty-four hour urine sample. However, as Turrell says, the presence of iodin in the urine does not confirm its deep penetration in the local area of application.

EXPERIMENT XI.—Human.

Purpose. To introduce I from NaI into a human subject.

Conditions. Voltage, 20; milliampèrage, 2; time, fifteen minutes.

Procedure. Five per cent NaI on negative pole; hand and wrist immersed. One per cent NaCl on positive pole; hand and wrist immersed.

Observations. The burning and tingling sensation at the positive pole is decidedly unpleasant.

Results. Urinalysis on three subsequent days were negative for iodin.

Remarks. This is contradictory to Bourguignon's findings. The number of milliampère minutes (10 ma. × 3 min. = 30 and 2 ma. × 15 min. = 30) are the same, hence theoretically a proportionate amount of iodin should be absorbed. The negative findings here can probably be attributed to the short duration of the experiment.

That iodin is electrolytically absorbed from the skin is an actuality. Witness the following protocol:

EXPERIMENT XV.—Rabbit; weight, 1.3 kg.

Purpose. To introduce I from KI through the skin by means of the galvanic current.

Conditions. Voltage, 20; milliampèrage, 7½; time, 2.45 to 4.45 P.M.

Procedure. Rabbit ears immersed. Potassium iodide (4 per cent, in negative beaker; sodium chloride (1 per cent) in positive beaker.

Results. 5.00 P.M.: Rabbit catheterized; urine gave strongly positive iodin test.

April 4, 1923. 10.00 A.M.: Urine positive for iodin.

April 5, 1923. 10.00 A.M.: Urine positive for iodin.

Controls. These were negative. Immersion of rabbit ears in a concentrated solution of iodin (5 per cent) in KI solution (4 per cent) for two hours, was not attended by sufficient absorption of iodin, to be detected by excretion in the urine.

Remarks. Iodin is readily absorbed through the skin from an ointment or alcoholic medium, but not from an aqueous solution. The galvanic current greatly facilitates the ingress of the iodin ion from the latter solution.

Detoxication of the Body by Means of the Electric Current. W. I. Morton suggested that, insomuch as ions can be driven in through the skin, a reversal of current might be an efficient means of detoxicating the body from such poisonous metals as lead and arsenic. This theoretical suggestion has found clinical expression in the so-called electrolytic treatment of lead poisoning, wherein the patient is partially immersed in a weak saline solution at the negative pole. We have been unable to find data confirming the exodus of lead.

Actuated by the above, we experimentally poisoned rabbits with mercuric acetate and attempted to withdraw some of the mercury ions through the skin of the ear of the rabbit. At frequent intervals the beaker at the negative pole was tested for mercury. In no instance was mercury found.

The hypothesis is without merit. The relative proportion of mercury or lead ions with the other ions normally present in the tissues is infinitely small. Must we suppose that the electrical charges have a specific affinity for the mercury or lead ions? This is manifestly untrue for two reasons. There are many ions (such as H ion) within the tissues that migrate with a much greater velocity than does lead or mercury, hence these would carry the majority of the electric charges. Again mercury and lead form somewhat insoluble organic salts (albuminates, etc) which do not ionize, and in addition remain intact within the body for a long period of time.

EXPERIMENT XVI.—Rabbit; weight, 1.5 kg.

Purpose. To detoxicate the body of the iodin from sodium iodide.

Conditions. Voltage, 20; milliampèrage, 10.

Procedure. Rabbit's ears were immersed in two separate beakers. Both beakers contained sodium chloride solution (1 per cent).

Positive electrode in one beaker and negative electrode in the other.

10.28: Five grams of sodium iodide in solution were given by stomach-tube. Samples of fluid were taken at intervals from the beaker at the positive pole and tested for iodin.

Observations. 10.55: No iodin demonstrable.

12.00: Very faint iodin test.

12.15: Definite positive starch test for iodin.

Remarks. This experiment was verified several times. The results are not as paradoxical as they may seem. The iodin ion migrates with a velocity equal to that of the chlorine ion. Furthermore the iodides exist in the circulating fluids as such and hence are available for ionic migration. The proportion of iodin to chlorin ion leaving the body to appear at the positive pole is, no doubt, the same as their relative ratio in the blood stream; so there is no selection of the iodin ions to carry the electrical charges, with the exclusion of all other ions. The human excretes some iodin in sweat; but because rabbits lack sudoriferous glands this withdrawal of iodin through the skin is all the more conclusive.

The Treatment of Experimental Infections by Electrolysis.—Pharmacologically, the iodides and nascent iodin behave differently. The latter is an efficient antiseptic, but does not exist in this form within the body. The positive pole electrolyzes the iodides releasing the resultant nascent iodin. This fact has been utilized clinically by Strandberg, later by Harris.[17]

Harris treated an extensive lupus ulceration as follows: The patient was given 3 gm. of NaI per os. After permitting sufficient time for the iodides to be well distributed throughout the tissues (seventy-five minutes), the positive pole (needle) was introduced into the lesion. A series of three-minute treatments, using a current of 2 ma., was required. The question here is whether or not sufficient nascent iodin is released to be of benefit.

EXPERIMENT X.—Cat; weight, 2.4 kg.

Purpose. The demonstration of free nascent iodin in muscles, by the insertion of the positive pole in the muscle, after sodium iodide has been taken by mouth.

Conditions. Voltage, 20; milliampèrage, 2.

Procedure. 4.00 P.M.: Paraldehyde (2.5 cc) and 5 gm. of potassium iodide in solution—given by stomach-tube.

4.15 P.M.: Muscle of thigh exposed and dilute starch solution injected intramuscularly. This was to permit sufficient time to elapse for the diffusion of tissue fluids and starch solution within the muscle.

4.30 P.M.: Negative electrode attached to opposite leg. Current turned on. Using platinum-wire electrode as the positive pole,

and introducing this terminal into the previously starched muscle, a definite blue coloration of the fluids occurred. This did not occur with other muscles. The color was distinctly blue and entirely different from the brown, charred areas of cautery that occasionally occur. This finding was corroborated in rabbits and white rats.

Experiments XIII, XXVI and XXVII.—White rats and rabbits.

Purpose. To produce localized infections in rats and rabbits, and to treat these with sodium iodide per os and electrolysis within the lesions.

Procedure. Suspensions of attenuated Staphylococcus pyogenes aureus cultures of low virulence were employed as the infecting organisms. Series of albino rats and rabbits were inoculated with the saline suspensions of these organisms; 0.05 cc and 0.1 cc of these suspensions were injected subcutaneously into rat and rabbit ears respectively by means of a tuberculin syringe. Definite tiny wheals appeared. As a rule, variable sized localized infections appeared at the site of inoculation. These differed considerably in severity of appearance. Well-marked lesions were present in the rat's ears within twenty-four to thirty-six hours; in the rabbit's, within forty-eight hours. Some of these untreated animals served as controls. Others were treated with the electric current alone, *i. e.*, with the positive pole needle in the infected lesion. In the remainder sodium iodide was given by mouth (rabbits) and hypodermatically (rats) and the current employed for electrolysis within the lesion. In some instances only one ear was used, the other serving as a control.

Results. These may be summarized. Those treated by the release of nascent iodin at the positive pole, implanted in the lesion, fared no better than the ears subjected to the influence of the electric current alone. Any beneficial effects, as compared with the controls, may be attributed to the phenomena occurring at the positive pole, other than the release of nascent iodin. These bactericidal phenomena are: The formation of heat, the release of nascent oxygen, the production of concentrated acid and the bacteriotropical influence of the positive pole for the negatively charged protoplasm of the staphylococci. Our results tend to validate the rationality of Fowler's[7] employment of the electrolytic bath in the treatment of septic wounds. He immerses the wound in a warm solution of NaCl and places the positive electrode in the bath. The stimulation of tissue regeneration and epithelial proliferation by the galvanic current is another modifying factor.

Discussion. Of what particular advantages can this method boast over other forms of administration? Clark[8] and other electrotherapeutists submit the following reasons. The drugs are not subject to the digestive changes which may accompany

oral administration. With hypodermic administration, the drug follows the course of the circulatory fluids and is quickly absorbed, whereas in the electrolytic absorption method the current dominates all osmotic conditions, and the cellular membranes are penetrated by the drug. Theoretically, then, in the latter instance the cells become more saturated with the medicament. This presents strong argument for the utilization of this method of therapy in local conditions, especially since it is not always advisable to distribute the drug throughout the body, when only a local area is in need of it. Moreover, larger quantities of the medicament can be applied to the local area under treatment. It is believed by some to be attended by a more prolonged local action, although we did not find this true with the local anesthetics. The disadvantages are the pain, inconvenience, danger of burns, variability in dosage, etc.

Several decades ago this phenomenon was entirely attributed to cataphoresis. This term implies an electrical osmosis, a liquid flow from anode to cathode. This is molecular rather than ionic. It is quite a slow process. Clinicians have attempted to absorb exudates and fluid accumulations by this fluid current. It may facilitate the migration of the cation but not the anion, because the fluid flow is from anode to cathode. The specific migrational velocity of the cation may be superimposed upon the speed of the cataphoretic current, giving a picture similar to that of a man walking forward on a moving train. Cataphoresis is at present largely disregarded.

The experiments cited here are in agreement, as a rule, with the work of Turrell in England and Clark in America. Both are agreed that "ionic medication" is indicated in local conditions. Although deep ionic medication is impossible (excluding circulatory transmission), beneficial results do accrue from the ionizing action of the current alone. Clark's[8] conclusions cannot be better stated: "The application of the galvanic current alone, without the use of remedial drugs, is often of benefit in various pathological conditions due to interpolar ionization of the tissue constituents, thereby altering nutrition, improving metabolism and producing stimulation or sedation, contraction or dilatation, depending upon the polarity of the current."

Conclusions. I. The electric current may be used as a means of driving ions into the skin. There are, however, various factors involved in this transfer, *e. g.*, the ampèrage used; the time of application; the resistance of the tissues; the migrational velocity of the entering ion, and also its chemical nature.

In the case of the heavy metals, as Hg^{++}, Mg^{++}, Zn^{++}, Pb^{++}, their ions as soon as they enter the skin give up their electrical charge to other much faster traveling ions present in the tissues, *e. g.*, H, Na. The metals, then, losing their charges, enter into

combination with the protein and salts of the tissues and may form precipitates. These are redissolved too slowly to be demonstrable by the common chemical tests in the excretions. Heavy metals, therefore, may be efficient for purely local administration, but not for systemic effect.

II. The electric current facilitates the introduction of many alkaloids through the skin.

(*a*) Systemic effects of strychnin and pilocarpin were demonstrated upon rabbits after electrolytic administration of the drugs for approximately one hour each. Controls without the current were negative.

(*b*) The action of caffein and curare (as gauged by systemic effects) failed to be demonstrated upon rabbits after electrolytic administration of the respective drugs for approximately two hours each.

(*c*) The action of curare, picrotoxin, strychnin, veratrin and nicotin was shown to be definitely accelerated when electrolytically introduced into frogs' skin, as compared with controls.

(*d*) Electrolytic experiments with local anesthetics in which a current of 2 ma. was used for ten minutes upon a human subject showed that:

1. Cocain produced moderate but incomplete anesthesia of finger lasting about one hour.
2. Procain and butyn produced mild anesthesia lasting about one-half hour.
3. Benzylcarbinol and salicain failed to produce any significant anesthesia.

III. Halogens, non-metals and acids, being anions are introduced by anaphoresis. The ingress of some is demonstrably accelerated by the electric current (CN, I_2), while in others there could not be demonstrated any acceleration of introduction by the electric current (NO_2, salicylates).

IV. The theory of detoxication of poisonous ions by electrolysis is fallacious. The application of an electric current is not specific for the egress of particular ions, except those with a relatively great migrational velocity (*i. e.*, H, Na, Cl_2, I_2). The migrational velocity of the ions of the common poisons, as the heavy metals and alkaloids, is very small as compared to that of the ions normally present in the tissue, and therefore the principle of detoxication cannot be applied to the former.

V. After the administration of iodides, per os or subcutaneously, nascent iodin can be liberated within the tissues by the insertion of a positive pole of an electrode. This principle may possibly be utilized in the treatment of certain infections. However, equally beneficial effects seem to be obtainable by the application of the electric current *per se*, as a result of the drastic tissue changes which are produced.

BIBLIOGRAPHY.

1. Alt and Schmidt: Electricity in Medicine, W. H. Guillemnot, p. 201.
2. LeBlanc, M.: A Text-book of Electrochemistry, The MacMillan Company, New York, p. 59.
3. Fette, G. T.: Jour. Nat'l Dental Assn., 1918, **5**, 1033.
4. Inchley, O.: Jour. Pharm. and Exp. Therap., 1921, **18**, 241.
5. Cross, H. V.: Arch. Radiol. and Electro., 1918–1919, **23**, 149.
6. Rolfe, W. A.: Boston Med. and Surg. Jour., 1919, **181**, 196.
7. Fowler: British Med. Jour., 1913, **1**, 922.
8. Clark, W.: Am. Jour. Electrotherap. and Radiol., 1919, **27**, 98.
9. Turrell, W. J.: Arch. Radiol. and Electro., 1922, **27**, 130.
10. Turrell, W. J.: Am. Jour. Electrotherap. and Radiol., 1920, **38**, 229.
11. Friel, A. R.: Practitioner, London, 1918, **101**, 315.
12. Friel, A. R.: Lancet, 1920, **199**, 345.
13. Borrel, A., de Coulon, M., and Boez, L.: Compt. rend. soc. de biol., Paris, 1922, **87**, 1118.
14. Wardle, M.: British Med. Jour., 1919, **2**, 495.
15. Jacoby, G. W.: A System of Physiological Therapeutics (edited by S. S. Cohen), Vol. II, Electrotherapy, P. Blakiston's Sons & Co., Philadelphia, 1902.
16. Bourguignon, G.: Arch. Radiol. and Electro., 1922, **27**, 139.
17. Harris, J. D.: Arch. Radiol. and Electro., 1920, **23**, 222.

STUDIES IN PANCREATIC FUNCTION. THE ENZYMIC CONCENTRATIONS OF DUODENAL CONTENTS IN HEALTH AND DISEASE.*

By C. W. McClure, M.D.

WITH THE COLLABORATION OF

Chester M. Jones, M.D., A. S. Wetmore,

AND

Lawrence Reynolds, M.D.

(From the Evans Memorial, Boston, Mass.)

The present communication deals with the principal results obtained from a study of the enzymic concentration of duodenal contents. The contents were derived from normal persons and those with pathological affections of the pancreas, liver or gastro-intestinal tract. The main purpose of the study was to devise methods for demonstrating the degree of activity of the external secretory function of the pancreas, and to apply those methods to the investigation of this function in various pathological conditions involving the gastro-intestinal tract, including the liver and pancreas.

Physicians are, naturally, most interested in that phase of laboratory investigation which develops methods which can be applied clinically. The development of such an investigation is very apt

* Presented, by invitation, to the American Gastro-enterological Association, Atlantic City, 1923.

to divide itself into the following three stages: (1) Devising of methods suitable for pursuing the problem; (2) application of the methods to the study of normal man; and (3) their application to the study of pathological conditions. These stages of development are exemplified by the present investigation.

Enzymic concentration was determined by estimating the activities of the proteolytic, lipolytic, and amylolytic enzymes of duodenal contents which were active in alkaline media. The methods used have already been presented in the *Archives of Internal Medicine*[1] and the *Journal of the American Medical Association*.[2] Proteolytic activity is estimated by allowing duodenal contents to act on a solution of casein. The casein not affected by the proteolytic enzyme is precipitated by means of metaphosphoric acid solution. The index of proteolytic concentration is taken as the number of milligrams of non-protein nitrogen left in solution by the metaphosphoric acid. This nitrogen is determined by an adaptation of the methods of Folin and Wu for the determination of non-protein nitrogen in the blood. Amylolytic activity is estimated as the number of milligrams of glucose developed by the action of a standard quantity of duodenal contents on a solution of soluble starch. The index of amylolytic concentration is taken to be the total number of milligrams of glucose developed, as estimated by the method of Folin and Wu for the determination of sugar in the blood. Lipolytic activity is estimated by allowing duodenal contents to act on a true emulsion of cottonseed oil and determining the amount of acidity developed by titrating with $^{N}/_{10}$ alcoholic NaOH solution. The total number of cc of $^{N}/_{10}$ NaOH necessary to neutralize the acidity developed is used as the index of lipolytic concentration. The duodenal contents and the reagents used must be controlled for the presence of nitrogen not precipitated by the metaphosphoric acid, for copper reducing bodies and for acidity.

The reason for the development of the methods described have been discussed in a previous communication.[1] For this reason it will suffice to state that the chemistry of all other methods is so grossly erroneous as to render the interpretation of results obtained by them well-nigh impossible.

Duodenal contents were obtained by use of the gastro-duodenal tube. The metal tip was allowed to pass through the pyloric sphincter and as far as the proximal end of the second portion of the duodenum. The position of the tube was ascertained by fluoroscopical observations. The subjects then reclined on the right side and the contents were obtained by siphonage.

Having devised methods, the next step was to apply them to the study of normal persons. The first study made on normal persons was that of the enzymic concentrations of duodenal contents collected while the stomach was in the fasting state. Duodenal contents collected under this condition showed marked variation in the

concentration of the various types of enzymes. These variations were found in specimens from the different subjects and in different specimens from the same subject. The findings are exemplified by those in the specimens of duodenal contents from two subjects which are outlined in the following table.

TABLE I.—ENZYMIC CONCENTRATIONS, AMOUNTS AND PHYSICAL CHARACTER OF FASTING-DUODENAL CONTENTS COLLECTED OVER THIRTY-MINUTE PERIODS

Subject.	Enzymic concentration.			Amount in cc.	Color.	Viscosity.
	Proteolytic in mg. NPN.	Lipolytic in cc N/10 NaOH.	Amylolytic in mg. glucose.			
C.	2.4	2.7	1.4	50	Pale greenish	Slight.
	1.2	0.4	0.6	135	Light brown	Moderate.
	1.8	0.5	0.3	15	Lemon-yellow	Slight.
	1.6	0.5	0.3	15	Lemon-yellow	Moderate.
	4.3	1.0	0.8	60	Lemon-yellow	Slight.
F.	2.5	0.4	1.6	58	Pale yellow	Slight.
	0.6	0.6	2.1	40	Pale greenish	Slight.

Although the fasting stomach contained no liquid or food ingested by the subjects, nevertheless in taking the tube subjects also swallowed much saliva. It is also well known that the fasting stomach contains more or less acid secretion, cellular débris and mucin. Undoubtedly, the stomach throws these materials over into the duodenum, so that a truly fasting state of the stomach and duodenum is not obtainable. Just what role the presence of these materials in the duodenum played in the production of the presence of enzymes in the duodenal contents was not determined. However, this does not detract from the accuracy of the observations, which were made on 22 different specimens of duodenal contents obtained from 6 normal persons. The amounts of these specimens varied from 29 to 135 cc, the color was some shade of pale yellow and the viscosity varied from slight to moderate. Proteolytic concentration varied from 1.2 to 5.0 mgs. of non-protein nitrogen, lipolytic concentration from 0.0 to 2.7 cc of NaOH, and amylolytic concentration from 0.3 to 6.7 mgs. of glucose.

A study was made of the effect of the ingestion of moderate sized meals on the enzymic concentration of duodenal contents. For this purpose a semi-solid meal of milk and cottage cheese, representing a mixed diet of protein, fat and carbohydrate, was used. The volume of the meal was 300 cc. It took about four hours for the stomach to empty itself of the meal, during which time duodenal contents were collected over hourly periods. The enzymic con-

centrations of the different hourly specimens were comparable; in other words, the concentrations did not show systematic increase from the first to the fourth hours. These findings demonstrated that hourly collections of duodenal contents contained enzymic concentrations representative of those occurring throughout the period of gastric digestion; *i. e.*, the time during which the stomach was emptying itself of food.

Further observation showed that an hourly specimen of duodenal contents derived from a meal of a volume of 50 cc contained enzymic concentrations comparable to those obtained by the use of meals of a volume of 300 cc. But comparable results could be obtained only if the collection time of the duodenal contents was proper, as will be described later on. The use of meals of small volume was practical both from the standpoint of the comfort of the subject and in lessening the laboratory work. For these reasons all the work which will be subsequently described was carried out with the meals of a volume of 50 cc.

The next studies were made on the effect of single pure food substances on the enzymic concentrations of duodenal contents. The food substances used were casein, edestin, olive oil, and arrowroot starch. Usually 10 or 25 gms. of one of these, or in the later experiments of mixtures of them, were made up to a volume of 50 cc with tap water and ingested by the subject. After its ingestion the food substance appeared in the duodenal contents either immediately or within a period of twenty minutes. Other than for the presence of this food stuff no apparent change occurred in the character of the duodenal contents and no increase in the enzymic concentrations, until the lapse of periods varying from ten to forty-five minutes. The change which then occurred was most striking and consisted of an abrupt change from a pale yellow color to some shade of dark brown or a very dark yellow. Coincident with the change in color the viscosity increased and, also, the enzymic concentrations. This was shown by study of the enzymic concentrations of fractions of duodenal contents collected over periods of fifteen minutes up to and during the hour succeeding the change to the dark colored bile. The enzymic concentrations of duodenal contents collected during this hour were found to be comparable to those collected over hourly periods after the ingestion of meals of a volume of 300 cc. During a part, at least, of this hour the food substance which had been ingested was passing out of the stomach and through the duodenum. However, the emptying time of the stomach was found to vary; sometimes the stomach emptied itself of the food substance in about an hour, while in other instances there would be a residue remaining at the end of two hours. When the emptying time of the stomach extended well into the second hour the enzymic concentrations of the duodenal contents were comparable to those collected during the first hour.

But if the stomach emptied during the period of the first hour of collection, the duodenal contents obtained during the second hour showed enzymic concentrations comparable to those obtained under fasting conditions. The time coincidence of the onset of the flow of bile and pancreatic juice suggests a common stimulant.

TABLE II.—ENZYMIC CONCENTRATIONS, AMOUNTS AND PHYSICAL CHARACTER OF DUODENAL CONTENTS COLLECTED OVER PERIODS I, II AND III.*

Subject.	Enzymic concentration.			Amount in cc.	Color.	Viscosity.	Kind of food ingested.	Period of collection.
	Proteolytic in mg. NPN.	Lipolytic in cc N/10 NaOH.	Amylolytic in mg. glucose.					
C. . .	3.9	2.3	1.4	30	Pale yellow	Slight	None	I
	0.0	0.2	0.0	50	Light yellow	Slight	Casein	II
	4.2	2.0	1.0	165	Very dark yellow	Moderate	Casein	III
F. . .	1.4	0.6	2.1	50	Light yellow	Slight	None	I
	0.8	0.3	1.2	40	Light yellow	Slight	Olive oil	II
	5.6	4.4	3.0	100	Dark brown	Moderate	Olive oil	III

* Period I, while the stomach was fasting; Period II, from immediately after the ingestion of food until the abrupt change to a dark-colored bile occurred; Period III, during the first hour after the abrupt change to dark-colored bile occurred.

Table II gives figures representing the concentrations of the three types of pancreatic enzymes in duodenal contents collected over the following periods: (I) While the stomach was fasting; (II) from immediately after the ingestion of a food substance until the abrupt change to a dark-colored bile occurred; (III) during the first hour after the change to dark-colored bile occurred. Study of the figures in Table II for the first two periods of collection shows that the concentrations of the various types of enzymes varied from very little to relatively great. On the other hand, it will be noted that none of the figures representing the enzymic concentrations of the third period of collection are less than whole numerals. This difference in magnitude of the minimum variations in enzymic concentrations sharply differentiates this one period from all others; and is well demonstrated in Table III.

Study of Table III demonstrated that fasting duodenal contents occasionally showed enzymic concentrations apparently comparable to those found in contents obtained during the third period of collection. But the fasting contents were relatively undiluted, while those collected after the ingestion of food were diluted with bile and gastric chyme. Amounts of the latter were particularly large after the ingestion of meals of a volume of 300 cc as judged both by the quantities of duodenal contents collected and the amounts

of barium seen to be ejected from the stomach into the duodenum when observed through the fluoroscope. For this reason the enzymic concentrations found in duodenal contents during the time the stomach was emptying itself of food represented greater concentrations of enzymes than were present in fasting duodenal contents. As has been stated, the enzymic concentrations of this third period of collection, after the ingestion of a meal of 50 cc volume, were comparable to those found in duodenal contents derived from meals of a volume of 300 cc. From these findings it is concluded that the presence of food in the stomach and duodenum in some way brings about the stimulation of the secretion of pancreatic juice, and that this stimulation is represented by an increase in the enzymic concentrations of duodenal contents collected during the third period of collection, as represented in Table III.

TABLE III.—MINIMUM AND MAXIMUM DEGREES OF ENZYMIC CONCENTRATIONS OF DUODENAL CONTENTS COLLECTED OVER PERIODS I, II AND III.*

Period of collection.	Enzymic concentrations.					
	Proteolytic in mg. NPN.		Lipolytic in cc N/10 NaOH.		Amylolytic in mg. of glucose.	
	Minimum.	Maximum.	Minimum.	Maximum.	Minimum.	Maximum.
Period I	1.2	5.0	0.0	2.7	0.3	0.7
	0.8	4.3	0.0	2.2	0.0	3.1
	2.7	5.7	1.0	4.4	2.5	4.5

* Period I, while the stomach was fasting; Period II, from immediately after the ingestion of food until the abrupt change to a dark-colored bile occurred; Period III, during the first hour after the abrupt change to dark-colored bile occurred.

The enzymes whose concentrations have been studied may be derived from sources other than the pancreas; *i. e.*, the stomach, duodenal mucosa and saliva. It is conceivable that ptyalin might reach the duodenum in active form; such an occurrence would increase the amylolytic concentration. Gastric lipase, if such an entity exists, would be present in negligible amount, judging from the small quantity said to be demonstrable in stomach contents; while pepsin is not active in the hydrogen-ion concentration used in the method for demonstrating proteolytic activity. While certain enzymes are demonstrable in the duodenal mucosa, their presence in the lumen of the gut has never been shown. Furthermore, diminution in enzymic concentrations was found under conditions which depressed pancreatic function, as will be demonstrated later on in this article. For these reasons it may be assumed that the concentrations of enzymes demonstrated by the methods used

in this investigation represented, very largely at least, enzymes secreted by the pancreas.

The work so far discussed has described the development of the procedures which gave results showing the effects of food on the enzymic concentrations of duodenal contents. The next step was to determine the comparative effects on enzymic concentrations of specific types of food substances. For this study 5 normal subjects were fed casein, edestin, olive oil or arrowroot starch. Each feeding experiment was done on a different day. The food substances were fed in 10-gm. amounts to 2 subjects and in 25-gm. amounts to three. The results are outlined in the following table (Table IV).

TABLE IV.—ENZYMIC CONCENTRATIONS AND PHYSICAL CHARACTER OF DUODENAL CONTENTS DERIVED FROM PURE FOOD SUBSTANCES, FED SINGLY AND IN COMBINATIONS.

Subject.	Enzymic concentrations.			Color.	Viscosity.	Kind of food ingested.
	Proteolytic in mg. NPN.	Lipolytic in cc n/10 NaOH.	Amylolytic in mg. glucose.			
A. . . .	3.9	2.4	4.5	Dark brown	Moderate	Olive oil, 10 cc.
	3.3	1.8	2.4	Brownish-yellow	Moderate	Edestin, 10 gm.
	2.4	1.4	2.5	Yellowish-brown	Moderate	Arrowroot starch, 10 gm.
	4.7	2.0	3.5	Dark-yellow brown	Moderate	Olive oil, 5 cc; edestin, 5 gm.
	5.0	0.7	2.9	Yellowish-brown	Moderate	Olive oil, 5.3 cc; edestin, 5.3 gm.; starch, 5.3 gm.
B. . . .	3.2	1.8	3.6	Very dark brown	Moderate	Olive oil, 10 cc.
	3.4	1.5	3.6	Dark brownish-yellow	Moderate	Edestin, 10 gm.
	3.0	1.0	3.3	Yellowish-brown	Moderate	Arrowroot starch, 10 gm.
	3.4	1.2	3.1	Brownish-yellow	Moderate	Arrowroot starch, 5 gm.; olive oil, 5 cc.
	4.3	0.0	2.7	Brownish-yellow	Moderate	Edestin, 5 gm.; arrowroot starch, 5 gm.
	2.1	0.8	2.1			
C. . . .	4.2	2.0	1.0	Yellow	Moderate	Casein, 25 gm.
	5.7	3.5	2.6	Blackish	Moderate	Olive oil, 25, cc.
D. . . .	3.5	1.4	3.5	Yellow	Moderate	Casein, 25 gm.
	3.5	3.3	4.3	Blackish	Moderate	Olive oil, 25 cc.
E. . . .	4.9	3.2	1.4	Yellow	Moderate	Casein, 25 gm.
	6.0	4.80	4.3	Blackish	Moderate	Olive oil, 25 cc.
F. . . .	5.6	4.4	3.0	Blackish	Moderate	Olive oil, 25 cc.

Study of Table IV shows that the concentration of lipase was greatest after the ingestion of olive oil, less after edestin or casein

and least after the ingestion of starch; in 2 of the subjects the food mixtures yielded duodenal contents showing still lower lipolytic concentration. These findings demonstrate a relationship between the kind of food ingested and the enzymic concentrations of duodenal contents.

Having established the effects of food on the enzymic concentrations of duodenal contents the next step in the investigation was to ascertain the effects of water drinking. For this purpose the fasting contents were collected for thirty minutes, then the subject was given 50 cc of tap water and the contents again collected for periods of forty-five minutes to one hour. In certain of the experiments the contents were collected over the period of a second hour. The enzymic concentrations found in the contents collected during the second hour were fully comparable to those obtained during the first hour. Experiments were carried out on 5 normal persons, and results obtained are exemplified in the following representative table (Table V). To this table are added figures representing the enzymic concentrations of duodenal contents derived from olive oil or edestin.

TABLE V.—ENZYMIC CONCENTRATIONS AND AMOUNTS OF DUODENAL CONTENTS COLLECTED FROM THE FASTING DUODENUM AND AFTER THE INGESTION OF TAP WATER, OLIVE OIL, EDESTIN OR CASEIN.

Subject.	Enzymic concentrations.			Amount in cc.	Duration of collection in minutes.	Kind of food ingested.
	Proteolytic in mg. NPN.	Lipolytic in cc N/10 NaOH.	Amylolytic in mg. glucose.			
C. . . .	1.8	0.5	0.3	30	30	Fasting duodenum.
	1.5	0.1	0.0	52	45	Tap water, 50 cc.
	4.2	2.0	1.0	165	60	Casein, 25 gm.; tap water, 25 cc.
	5.7	3.5	2.6	100	60	Olive oil, 25 cc; tap water, 25 cc.
B. . . .	1.9	1.1	1.8	25	30	Fasting duodenum.
	3.0	0.5	2.0	60	60	Tap water, 50 cc.
	2.7	1.5	2.5	140	60	Edestin, 10 gm.; tap water, 40 cc.
	3.2	1.8	3.6	270	60	Olive oil, 10 cc; tap water, 40 cc.

As the above table shows, enzymic concentrations were diminished in some cases after the ingestion of water, possibly by dilution. On the other hand, the concentration of one type of enzyme might be increased, while that of the other types remained approximately the same or was diminished; the resultant figures expressing enzymic concentration were comparable to those obtained for fasting con-

tents. The table, also, shows that the enzymic concentrations of duodenal contents were much greater after the ingestion of food than after water. These findings demonstrate very definitely that water was a less potent stimulant to the secretion of pancreatic juice than was food. They present further evidence that the enzymic concentrations of duodenal contents were influenced by the kind of material ingested.

Studies of the hydrogen-ion concentration of duodenal contents were made after the ingestion of meals of 300 cc and of 50 cc volume. The large meals were composed of milk and cottage cheese or of 20 per cent cream; the small meals were of olive oil or edestin. The hydrogen-ion concentration was found to vary from 3 to 8; and no relation was found to exist between the degrees of acidity and the magnitude of enzymic concentrations. In fact, the duodenal contents from the cream or olive oil were often alkaline; but, nevertheless, showed as a rule, enzymic concentrations greater than were found in acid contents derived from protein or carbohydrate meals.

The findings which have been discussed in the present investigation are of interest in relation to the various theories concerning the mechanism by which the external secretory activity of the pancreas is stimulated.

As has been discussed, evidence of pancreatic stimulation was much less pronounced after the drinking of water than after the ingestion of foodstuffs. This finding occurred in spite of the fact that water stimulates the secretion of acid gastric juice; so that after its ingestion acid fluid was ejected from the stomach into the duodenum. From this it is concluded that something more than the mere ejection of acid contents into the duodenum is necessary to stimulate materially pancreatic secretion. It was also demonstrated that a relation existed between the degrees of enzymic concentration and the kind of footstuff ingested; while on the other hand, no relation was found between the magnitude of enzymic concentration and the degree of acidity of the duodenal contents. The findings, therefore, present evidence that the acidity of duodenal contents is not the essential factor causing the stimulation of pancreatic juice in man.

It will be recalled that, after the ingestion of food and its appearance in the duodenal contents, a period existed during which digestion and absorption of the digested products could occur. Therefore, the finding: (1)That food in some way stimulated the secretion of pancreatic juice; (2) that a relation existed between the degrees of enzymic concentration and the kinds of food ingested; (3) that a latent period existed in which the foodsuffs could be digested and absorbed; and (4) that water was a much less potent pancreatic stimulant than food, although water stimulates a normal gastric acidity, present evidence that the products of food digestion are an essential factor in stimulating the secretion of pancreatic juice.

The above interpretation of the findings in the experimental work here reported do not agree with the view of Pawlow,[4] except for lipolytic activity. They do not uphold either the secretin theory of Bayliss and Starling[5] nor the hypothesis of a nervous mechanism as the most potent factors in the stimulation of pancreatic juice. The remaining most probable possibility is that the products of the digestion of food are the essential factor in stimulating the pancreas to secretory activity in man.

The disagreement with Pawlow's contentions may possibly be more apparent than real. In the first place Pawlow worked on dogs; and a pancreatic regulatory apparatus may exist in dogs which is different from that of man. In the methods used by Pawlow for demonstrating enzymatic activity the substrates acted upon by enzymes were placed directly into the pancreatic juice. The hydrogen-ion and buffer conditions of the various specimens of pancreatic juice may have been such as to give results justifying Pawlow's conclusions. But the physical chemistry of Pawlow's methods is so grossly erroneous that an interpretation of results by them is well-nigh impossible.

The experiments of Bayliss and Starling[5] consisted in the intravenous injection into animals of hydrochloric acid extracts of duodenal mucosa. In this way pancreatic secretion was stimulated. But the work of von Fürth[6] clearly demonstrates that it is not necessary to assume the existence of "secretin" to explain this stimulation. This investigator, among others, has demonstrated that various well-known chemical substances normally present in duodenal mucosa will produce such a stimulation. Furthermore, the maceration of duodenal mucosa and its extraction with hydrochloric acid might very well form compounds (due to decomposition of proteins, etc.) similar to those occurring during digestion; such compounds may play a role in the stimulation of pancreatic juice when injected into the blood-stream of an animal. In other words, the chemistry of the work of Bayliss and Starling was such as not to justify the drawing of far-reaching conclusions from their observations.

Experiments have been repeatedly carried out by the present authors in which water, $^{N}/_{20}$ HCl, glucose solutions and olive oil have been introduced directly into the duodenum of men. The results were the same as those obtained after the ingestion of these substances by mouth. Certainly these substances were introduced in an inert chemical state, except the $^{N}/_{20}$ HCl. This contradicts the often-quoted statement that such substances do not stimulate pancreatic secretion. From these experiments it was concluded that whenever any harmless liquid is introduced into the duodenum of man, intestinal digestion and absorption may begin.

The absorption of materials present in the duodenal contents and those coming into the duodenum from the stomach, for in

man the introduction of fluid into the duodenum always starts up the ejection of stomach contents into the duodenum as the authors have repeatedly demonstrated, could explain the often quoted experiment of Popielski.[7] In this experiment hydrochloric acid solution was placed in the duodenum of one dog, whose blood supply was connected to that of another dog; as a result pancreatic juice was secreted by the latter. The contamination of the original duodenal material with gastric contents introduces an element of uncertainty, as digestible material thus present would give rise to products analogous to those produced by food digestion. In fact all the work supporting the "secretin" theory furnishes only indirect evidence of the correctness of that theory; while phenomena urged in its support can all be explained in other ways.

This discussion is not intended to belittle the excellent work of two such competent experimenters as Drs. Bayliss and Starling. But the purpose is to emphasize that "secretin" remains a hypothetical substance. Furthermore, it should be emphasized that the work on "secretin" has all been carried out on the lower animals; and whether or not the same experimental results would be obtained in man has not been determined.

The next phase of the investigation deals with the enzymic concentration of duodenal contents in diseased conditions of the pancreas, liver and gastro-intestinal tract.[8] Under such conditions bile was frequently not present in the duodenal contents. As a result, the criteria previously used for the time of beginning the collection of duodenal contents suitable for enzymic concentration studies were absent. Because of this it was necessary to find a type of meal that would stimulate the flow of pancreatic juice within a few minutes after its entrance in the duodenum. This was accomplished by a meal consisting of 50 cc of 20 per cent cream, containing 15 grams of barium sulphate. The addition of barium sulphate allowed the behavior of the meal to be observed through the fluoroscope and it, also, frequently hastened the time of ejection from the stomach into the duodenum. The latter result was apparently a mechanical one, brought about in that the weight of the barium aided in getting the cream quickly into the pyloric region of the stomach.

The technic used in obtaining duodenal contents from pathological subjects is as follows: The duodenal tube was allowed to enter the second portion of the duodenum. The subject then ingested the meal described and reclined on the right side. The flow of duodenal contents was initiated by gentle aspiration with a syringe and as soon as cream and barium were obtained the collection was begun. The period of collection was one hour.

The minimum figures for the enzymic concentrations of duodenal contents derived from normal persons, after the ingestion of the meal and cream, were as follows: Proteolytic, 2 mgs. non-protein

nitrogen; lipolytic, 1 cc $^{N}/_{10}$ NaOH; and amylolytic, 1 mg. of glucose. The figures were the minimum figures, also, for enzymic concentrations of duodenal contents derived from patients with a variety of non-febrile diseases, and in whom there was no reason to suspect pancreatic involvement.

Among the pathological conditions studied were cases of diabetes mellitus, pernicious anemia, and achylia gastrica. The findings of normal enzymic concentrations in these cases are of both pathological and physiological interest. From the clinical standpoint, they exclude non-pancreatic conditions as factors affecting the enzymic concentrations of duodenal contents. Physiologically, the findings in achylia gastrica bear on the question of the secretin theory. In spite of the fact that in the cases studied, Toepfer's reagent failed to demonstrate the presence of hydrochloric acid in the gastric secretions, normal enzymic pancreatic function was found. This finding indicates that hydrochloric acid is not an essential factor in stimulating the secretion of pancreatic juice in man.

Study was made of the enzymic concentration of duodenal contents from patients in whom organic pancreatic disease was demonstrated at laparotomy or autopsy. The concentrations found fall into three clases, as follows: (1) Normal; (2) abnormally low; and (3) an intermediate value between those two.

1. Normal concentration was found in acute or chronic destructive lesions which did not involve the head of the pancreas; for example, destruction of the body and tail of the pancreas by cancer, but without involvement of the head of the organ.

2. Abnormally low concentrations were found in two types of conditions as follows: Destructive lesions involving the head of the pancreas, such as cancer of the head of the pancreas or acute pancreatic necrosis; and chronic pancreatitis with or without extensive involvement of the glandular parenchyma.

3. The intermediate value between normal and abnormally low concentrations was characterized by normal concentration of one or two enzymes while the other one or two was much diminished below the minimum normal; *i. e.*, dissociation of the concentrations of the various types of enzymes occurred. This was found in the duodenal contents of patients convalescing from acute pancreatic necrosis. Findings representative of these described are outlined in the table on page 661.

In studying patients with disease of the biliary tract the duodenal enzymic concentrations were found to fall into the same three classes described for pancreatic diseases; *i. e.*, normal, abnormally low, and intermediate or dissociated.

Normal concentrations of duodenal enzymes were found where no obstruction to the pancreatic duct existed. The concentrations were apparently not affected by the presence of bile or by its partial or complete absence in the duodenal contents. The patients studied were those with cancer of the bile ducts and partial or

complete obstruction of the common duct due to stone, the pancreatic duct not being affected. Three of the patients had been diagnosed clinically as cancer of the head of the pancreas. In the duodenal contents from 1 of these patients no bile pigment was observed; while the contents from the other 2 were pale green in color. The findings of normal enzymic concentrations in these cases cast doubt on the diagnosis of pancreatic malignancy, and on laparotomy stone in the common duct was found in each case.

TABLE VI.—ENZYMIC CONCENTRATIONS, AMOUNTS AND PHYSICAL CHARACTER OF DUODENAL CONTENTS OBTAINED FROM PATIENTS WITH DISEASE OF THE PANCREAS.

Subject.	Enzymic concentration.			Amount in cc.	Color.	Viscosity.	Diagnosis.
	Proteolytic in mg. NPN.	Lipolytic in cc. n/10 NaOH.	Amylolytic in mg. glucose.				
1x . .	2.5	1.6	2.0	90	Greenish-yellow	Moderate	Cancer body and tail pancreas.
2x . .	0.0	0.2	2.0	55	White	Great	Cancer head of pancreas.
3x . .	0.8	0.3	0.3	50	Yellow	Moderate	Chronic pancreatitis.
	1.1	0.3	0.5	60	Yellow	Moderate	
4x . .	1.9	0.7	1.9	150	Yellow	Moderate	Acute pancreatitis; convalescing.
	5.0	0.2	0.4	100	Yellow	Moderate	

x, Exploratory laparotomy.

Abnormally low and dissociated concentrations were found when the lesion obstructing the common duct involved the pancreatic duct also. With one exception, this lesion was stone in the ampulla of Vater. The exception noted was one in which sclerotic processes almost occluded the common bile duct.

Three of the cases studied are worthy of special mention. In these cases calculi obstructed the ampulla of Vater, and on the first examination the duodenal enzymic concentrations were much below the normal; while no bile was seen in the duodenal contents from 2 of the cases, and from the third were a pale green color. After lavage with magnesium sulphate solution a few times the duodenal contents showed bile pigment and normal enzymic concentrations. On the other hand, in 4 cases of cancer involving the bile ducts repeated lavage of the duodenum failed to be followed by bile in the duodenal contents. Two of the cases represented cancer of the head of the pancreas involving the pancreatic duct and lavage did not produce a change in the abnormally low enzymic concentrations. In the other 2 the pancreatic duct was not involved and the enzymic concentrations were normal. In these cases the use of magnesium sulphate lavage, combined with study of enzymic con-

centrations, of the duodenal contents gave findings in the presence of benign obstruction which were different from those obtained when the obstruction was of malignant character. The differences were so marked as to suggest that results obtained from the combined use of duodenal lavage and enzymic concentration studies will prove to be of value in differentiating between the two types of obstruction.

In obstructive jaundice the question frequently arises as to whether the cause is benign or malignant. The three most frequent malignant diseases causing jaundice are primary cancer of the head of the pancreas, primary cancer of the bile ducts, and cancer of the liver secondary to gastric carcinoma. The latter can almost invariably be demonstrated by Roentgen-ray examination of the stomach; cancer of the bile ducts does not allow bile to flow into the duodenum; and cancer of the head of the pancreas will usually occlude the pancreatic duct and largely exclude enzymes from the duodenum. Thus the estimation of duodenal enzymic concentrations would seem to be of distinct value in the diagnosis of a suspected cancer of the biliary tract or of the head of the pancreas.

The findings in biliary disease, which have been discussed, are exemplified in the following table (Table VII)

TABLE VII.—ENZYMIC CONCENTRATIONS, AMOUNTS AND PHYSICAL CHARACTER OF DUODENAL CONTENTS OBTAINED FROM PATIENTS WITH DISEASE OF THE BILIARY TRACT.

Subject.	Enzymic concentration.			Amount in cc.	Color.	Viscosity.	Diagnosis.
	Proteolytic in mg. NPN.	Lipolytic in cc N/10 NaOH.	Amylolytic in mg. glucose.				
1x . .	9.0	4.0	2.0	150	Yellow	Moderate	Cholelithiasis; no obstruction.
2x . .	2.7	1.6	0.7	100	Pale yellow	Great	Stone in common duct; deep icterus.
3x . .	2.0	0.2	0.6	50	White	Great	Stone in ampulla; deep icterus.
	3.9	1.0	0.9	70	Pale yellow	Moderate	After lavage with $MgSO_4$.
4x . .	1.0	0.1	0.0	150	White	Great	Stone in ampulla; deep icterus.
	5.9	1.9	3.3	100	Greenish-yellow	Moderate	After lavage with $MgSO_4$.

x, Laparotomy.

The effects of biliary and pancreatic diseases on the enzymic concentrations of duodenal contents, which have been discussed, may be summarized as follows:

(*a*) Abnormal enzymic concentrations were found in lesions

obstructing the pancreatic duct or causing extensive damage to the head of the pancreas. The lesions studied were acute pancreatitis, cancer of the head of the pancreas, and obstruction to the pancreatic duct by gall stones or by sclerotic processes.

(*b*) Abnormal enzymic concentrations were also found in chronic pancreatitis in which there was but little destruction of the glandular parenchyma.

(*c*) Normal enzymic concentrations were found when the lesion involved but little of the glandular parenchyma, when the pancreatic duct was not obstructed, and when the cause for an obstructive jaundice did not involve the pancreas or its duct.

The question arises as to the need for the rather complicated and time-consuming processes of obtaining and of estimating the enzymic concentrations of duodenal contents. It has been urged that any secretory anomalies of the pancreas would be reflected in the stools, and that the examination of the stools would suffice. That such is not necessarily the case is evidenced by the findings in a case of chronic pancreatitis, in which careful stool examinations were made on successive days following a Schmidt test diet. All examinations were negative. In several of the other cases studied the stool examinations on house diet showed no evidences of abnormal digestion. In cases with a low sugar tolerance, furthermore, it is obviously inadvisable to feed test diets of a character satisfactory for stool examinations. Also, examination of stools will be of no aid in the diagnosis of pancreatic disease when bile is excluded from the intestines or when pathological conditions prevent the absorption of food from the small intestines. In addition, it is well known that bacteria always present in human intestines can duplicate all phases of enzymic digestion, so that it is conceivable that bacterial action alone could mask evidence of pancreatic disease as obtained from stool examination. In this connection it is of interest to note that McClure, Vincent and Pratt[9] found that completely depancreatized dogs could often utilize a considerable percentage of fat of the food ingested. It seems clear, therefore, that pancreatic disease may not be evidenced by stool findings alone. For this reason in selected cases the use of the methods described and used in this work will be found of aid in the diagnosis and in following the progress of a given case.

Conclusions. 1. Normal enzymic concentrations of duodenal contents have been established for the methods and procedures described for estimating enzymic concentrations in duodenal contents obtained by the use of the procedures described.

2. Abnormalities in enzymic concentrations having been found only in the presence of some lesion involving the pancreas, either primarily or secondarily, it is concluded that the estimation of enzymic concentrations of duodenal contents furnishes an index to the activity of the external secretory function of the pancreas.

3. The findings in normal persons indicate that the essential

factors in stimulating the secretion of pancreatic juice are the products of digestion rather than the acidity of the gastric chyme.

4. The time coincidence of the onset of the flow of bile and pancreatic juice suggests a common stimulant.

5. The external secretory function of the pancreas, as measured by the enzymic concentration of duodenal contents, was found to be much depressed below the normal in chronic pancreatitis.

6. Acute pancreatic necrosis, cancer of the head of the pancreas, and lesions obstructing the pancreatic duct were accompanied by marked abnormalities in the enzymic concentrations of duodenal contents. Obstructive lesions caused great diminution, while acute necrosis often caused dissociation of the concentration of the enzymes.

7. In obstructive jaundice estimation of enzymic concentration of duodenal contents is of aid in localizing the site of the lesion, and in the differential diagnosis between its benign malignant character.

BIBLIOGRAPHY.

1. McClure, C. W., Wetmore, A. S., and Reynolds, L.: Arch. Int. Med., 1921, **27**, 706.
2. McClure, C. W., Wetmore, A. S., and Reynolds, L.: Jour. Am. Med. Assn., 1921, **87**, 1468.
3. McClure, C. W., and Wetmore, A. S.: Boston Med. and Surg. Jour., 1922, **187**, 882.
4. Pawlow, I. P.: The Work of the Digestive Glands, London.
5. Bayliss, W. M., and Starling, E. H.: Jour. Physiol., 1902, **28**, 325.
6. Von Fürth, O., and Schwartz, W. W.: Pflüger's Arch. f. d. ges. Physiol., 1908, **124**, 427.
7. Popielski: Zentralbl. f. Physiol., 1906, **19**, 801.
8. McClure, C. W., and Jones, C. M.: Boston Med. and Surg. Jour., 1922, **187**, 909.
9. McClure, C. W., Vincent, B., and Pratt, J. H.: Jour. Exp. Med., 1917, **25**, 381.

THE OCCURRENCE OF REGULAR VENTRICULAR RHYTHM WITH A RATE OF OVER FIFTY IN CASES OF AURICULAR FIBRILLATION.

By W. Dock, M.D.,
and
S. A. Levine, M.D.,
Boston.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.)

Auricular fibrillation, once established in cases of organic heart disease, usually gives a constant and persisting arrhythmia. Certain drugs may restore the normal mechanism, but under the continued use of digitalis the spontaneous return of normal action is unusual. However, not infrequently the examiner notes that

"the heart action is regular" or "more regular." It is, therefore, of importance to remember that in many such cases graphic records show persisting fibrillation of the auricle. This mechanism was first described by Lewis[1] and Mackenzie;[2] in the former instance the ventricular rate was regular at 85 to 90 beats per minute and in the latter it was 70. Lewis[3] regarded the condition as complete block and says: "In such instances the ventricular rate is relatively high, usually 40 to 50 per minute, but occasionally as high as 90 per minute, presumably because the block occurs at a high level in the *A–V* node and because the ventricle is governed by a rhythm formed in the *A–V* node."

There are numerous accounts[4–11] of regular ventricular rhythm in auricular fibrillation, with and without digitalis, in which the ventricular rate was below 50 per minute. Such cases are easily recognized as complete heart-block. With the more rapid rate, the actual condition is not recognized clinically, and it is important to know that in this clinic during the past ten years there have been 12 cases of auricular fibrillation studied with the electrocardiograph in which regular ventricular rhythm occurred after full doses of digitalis, with a rate between 55 and 85, the average rate being 68 per minute. During this time there were 614 cases of auricular fibrillation, 9 of which had periods of regular ventricular rhythm, with rates under 48. There were during the same time 16 cases of complete heart-block with regularly beating auricles. In 12 of the latter cases of complete heart-block, with no digitalis, the average rate was 35.8 beats per minute, while in 5 such cases treated with full doses of digitalis the average rate was 42.6. The maximum rate in the former group was 45 and in the latter, 60. In 1 case, included in both series, the rate was 34 without digitalis; six months later, following cardiac failure and continued use of digitalis, the ventricular rate was 55; the auricular rate had fallen from 115 to 90 beats per minute. This suggests that digitalis accelerates the ventricular pacemaker when there is *A–V* dissociation.

As we have seen it, regular and fairly rapid ventricular rhythm occurs in auricular fibrillation only after full doses of digitalis. It is always transient, lasting for hours or days. It may disappear and return later at a different rate, or the rate may vary from day to day. It seems to occur most often in badly damaged hearts. Half of our cases had severe mitral or aortic lesions, rheumatic in origin; 1 had syphilitic aortitis and others had myocardial failure without valve disease. Five died within one year of the time of observation.

Summary of Case Histories. CASE I.—Medical, No. 4036. Chauffeur, aged thirty-two years. Rheumatic fever at sixteen years; dyspnea for three years; orthopnea for one year; precordial

pain for two weeks. Apex in axilla; apical diastolic rumble and systolic murmur; liver slightly enlarged; legs not edematous. Discharged improved in eleven days. Diagnosis: Mitral stenosis and insufficiency.

CASE II.—No. 4727. Laborer, aged fifty-two years. Dyspnea and swelling of the legs for one year. Very large heart; liver just palpable; very slight edema of the ankles; blood-pressure, 244/170. Died in ninety-two days. Diagnosis: Chronic myocarditis, chronic nephritis and hypertension.

CASE III.—No. 5031. Butcher, aged seventy-two years. Ascites and edema of the legs for four months; orthopnea for two months. Apex in the axilla; sounds weak. Liver palpable; blood-pressure, 160/130. Died in ten months. Diagnosis: Chronic myocarditis.

CASE IV.—No. 5435. Fireman, aged sixty-five years. Orthopnea for five months; swelling of the ankles for six weeks. Heart enlarged; right hydrothorax; moist rales at the bases of the lungs; liver not felt; edema to mid-thigh; blood-pressure, 200/120. Discharged improved in twenty-eight days. Diagnosis: Chronic myocarditis and hypertension.

CASE V.—No. 5439. Housewife, aged forty years. Chorea and rheumatic fever in childhood; orthopnea for two years. Apex in axilla; apical diastolic thrill and murmur. Liver slightly enlarged ankles swollen. Died in two months. Diagnosis: Mitral stenosis and insufficiency.

CASE VI.—No. 6278. Housewife, aged forty-eight years. Rheumatic fever at twelve years; cyanotic for twelve years; dropsy for four months. Heart large; aortic systolic thrill and murmur. Liver edge at the navel; edema to the waist. Discharged improved in thirty-six days. Diagnosis: Aortic stenosis.

CASE VII.—No. 6845. Teamster, aged fifty-two years. Dyspnea for four months; orthopnea and swelling of the ankles for two months. Heart enlarged; presystolic gallop at the apex. Liver palpable, ascites and edema of the ankles. Moist rales at both bases. Discharged improved in thirty-six days. Diagnosis: Chronic myocarditis.

CASE VIII.—No. 6865. Printer, aged fifty-seven years. Dyspnea for four months; swelling of the legs and orthopnea for one month. Heart slightly enlarged; sounds faint. Rales throughout the lungs; edema of the legs and back. Died in fourteen days. Diagnosis: Chronic myocarditis.

CASE IX.—No. 6945. Housewife, aged thirty years. Rheumatic fever at thirteen years; dyspnea and precordial pain for two years; swelling of the abdomen and legs for two months. Heart slightly enlarged; diastolic rumble and presystolic murmur at the apex. Liver edge at the navel; marked ascites and edema of the legs. Died in twenty-one days. Diagnosis: Mitral stenosis and insufficiency.

CASE X.—No. 7101. Teacher, aged fifty years. Dyspnea for two months; precordial pain for one month; edema of legs for three weeks. Heart enlarged; loud systolic murmur all over precordium; short diastolic murmur at the apex; gallop rhythm. Large pulsating liver; edema of the legs and back; moist rales throughout the lungs; blood-pressure, 140/80. Discharged improved in fifty days. Diagnosis: Chronic myocarditis and aortic insufficiency.

CASE XI.—No. 13759. Stoker, aged fifty-seven years. Chancre at twenty-two years. Dyspnea for one year. Heart enlarged; loud aortic systolic and diastolic murmurs. Moderate ascites and edema of the legs; Wassermann, 4+. Discharged improved in thirty-six days. Diagnosis: Syphilitic aortitis and aortic insufficiency.

CASE XII.—No. 20712. Domestic, aged fifty-four years. Palpitation for five years; shortness of breath for two years. Night-sweats and productive cough for three weeks. Heart slightly enlarged; nor murmurs; very many moist rales throughout the lungs; blood-pressure, 155/70. Discharged improved in sixty-six days. Diagnosis: Chronic myocarditis.

The records of these 12 cases were diagnosed and filed as "complete heart-block," but the rapidity of the ventricular rate was noted and an attempt made to see if this might not be better explained by another mechanism. It seemed possible that in these cases there might be a high-grade partial block, due to digitalis, with the ventricle responding, for example, to every fifth or sixth impulse originating in the auricle, and that, as in certain instances of flutter, the block might be varied by changes in vagus tone. In the 2 cases, in 1916, vagal pressure produced no change in the rate of the ventricle. It was assumed at that time that the fibrillating auricle was absolutely irregular as distinguished from the very regular rhythm of the auricle in flutter, but the work of Lewis and his co-workers,[12, 13] on the circus movement of the auricular impulse has shown the very close analogy between the two conditions. It, therefore, seemed worth while, in reporting these cases,

to reëxamine the tracings for any evidence of similarity between the mechanism of these hearts and that of auricular flutter with a regular ventricular rhythm.

Case No.	Day in hospital.	Total amount of digitalis to date of observation.	Auricular mechanism.	Ventricular mechanism.	Ventricular rate per min.
		Grams.			
1. . .	1	0	Fibrillation	Irregular	100
	3	1.2	Fibrillation	Regular	73
	4	1.2	Fibrillation	Regular	73
	7	1.2	Fibrillation	Regular	57
2. . .	1	0	Fibrillation	Irregular	80
	58	4.5	Fibrillation	Irregular	90
	65	5.05	Fibrillation	Regular	81
	75	5.05	Fibrillation	Irregular	68
3. . .	1–7	0–2.45	Flutter	Varying block	100–130
	8 A.M.	0–2.45	Fibrillation	Irregular	52
	8 P.M.	2.65	Fibrillation	Regular	60
	9–20	2.65	Fibrillation	Irregular	48–62
	20–29	2.65–7.05	Flutter	Varying block	80–140
	30	7.15	Fibrillation	Regular	42
	31–38	7.15	Fibrillation	Irregular	39–60
	39	7.15	Regular	Regular	85
4. . .	1	Tincture to nausea	Fibrillation	Regular	85
	4–9	0.40–0.75	Fibrillation	Coupled	68–76
	11–21	0.75–1.55	Fibrillation	Irregular	54–61
5. . .	1–7	0.1	Fibrillation	Irregular	125–90
	10	1.7	Fibrillation	Regular	66
	26	2.8	Fibrillation	Irregular	90
6. . .	1	Digalen, gtts. v b.d. (2 mos.)	Fibrillation	Regular	58
	6	Digalen, gtts. v b.d. (2 mos.)	Fibrillation	Irregular	45
7. . .	1	0	Fibrillation	Irregular	150
	4	2.5	Fibrillation	Irregular	80
	6	2.5	Fibrillation	Regular	88
	26–36	2.5–3.4	Fibrillation	Irregular	83–90
8. . .	3	2.1	Fibrillation	Regular	56
	5–9	2.1	Fibrillation	Irregular	85–105
9. . .	1	0	Regular	Regular	108
	6	1.3	Regular	Dropped beats	80
	7	1.3	Fibrillation	Regular	68
	8–9	1.3	Fibrillation	Irregular	70–75
	15	2	Fibrillation	Coupled	94
10. . .	3	0.9	Fibrillation	Irregular	75
	7	2.1	Fibrillation	Regular	75
	21 A.M.	2.9	Fibrillation	Irregular	72
	21 P.M.	2.9	Fibrillation	Regular	75
11. . .	3	0	Regular	Regular	90
	7	3.0	Fibrillation	Regular	58
	11	3.0	Regular	Dropped beats	65
	22	3.0	Regular	Regular	88
12. . .	1	0	Fibrillation	Irregular	155
	3	1.6	Fibrillation	Irregular	65
	22	3.85	Fibrillation	Regular	59
	28	4.45	Fibrillation	Regular	58
	31–66	4.45–6.0	Fibrillation	Irregular	50–70

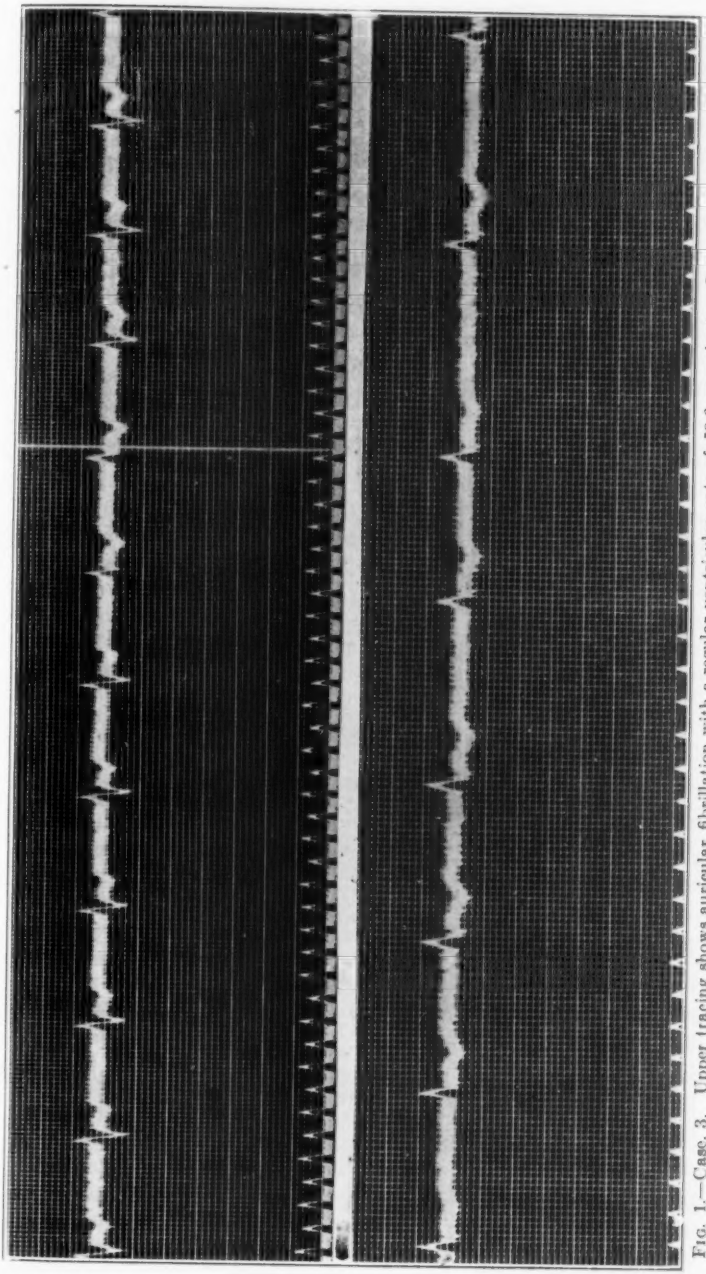


FIG. 1.—Case. 3. Upper tracing shows auricular fibrillation with a regular ventricular rate of 59.6 per minute. Lower tracing taken thirty-six hours later shows irregular ventricular rhythm rate 55.9.

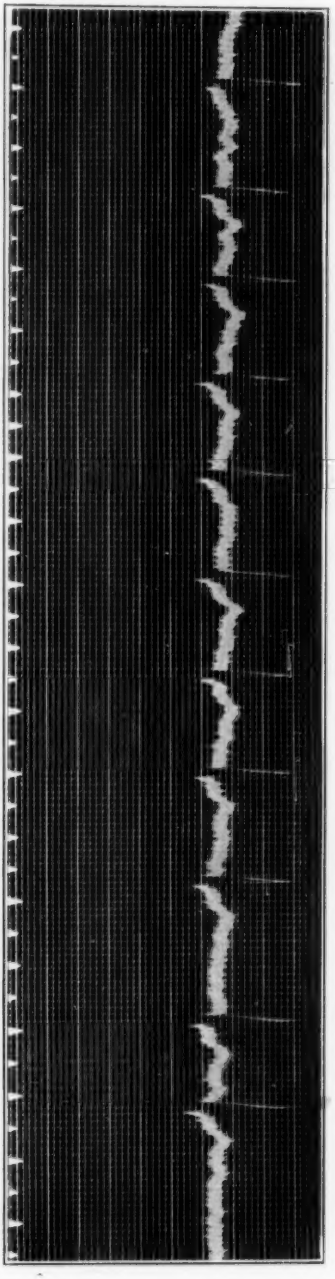


FIG. 2.—Case 1. Tracing shows auricular fibrillation with irregular ventricular response. Note constant length of five cycles in the center. Numbers above indicate interventricular intervals.

In Cases I and III right and left vagal pressure caused no variation in the ventricular rate. In Case XII, holding the breath, right and left vagal and ocular pressure and the subcutaneous injection of 3 mg. of atropin had absolutely no effect on the rate of the ventricle. Even if we should succeed in later cases in thus changing the rate, the existence of partial block will not be demonstrated since, as Hewlett[14] has indicated, the rhythm originating in the *A–V* node may be extremely susceptible to vagus influence. Until it can be shown that there is a direct relation between the rate of auricular impulses in fibrillation (*f* waves) and the ventricular rate, there is still lacking the proof of the view that such cases are instances of partial block. Measurements of our records for evidence of a simple ratio between the fibrillation rate and the ventricular response were wholly unsatisfactory. In 7 cases the *f* waves were too fine to be of any value, while in others, including Case XII, in which various sternal leads were taken, the *f* waves were so irregular that no comparisons could be made. Successive waves varied by 0.03 second, and groups of three successive waves varied by as much as 0.05 second.

In half of these cases (see table) the resumption of the irregular rhythm was associated with a decrease in the ventricular rate (Fig. 1), and if we reject the hypothesis of partial block we must assume that digitalis accelerated the rate of the dissociated ventricles. This is confirmed by the relatively more rapid ventricular rate in those cases of complete heart-block with normally beating auricles when under digitalis as compared with similar cases not treated with digitalis, as noted above.

One is struck by the fact that, in reverting to an irregular rhythm, these hearts often give tracings in which, mingled with beats of varied length, runs of beats of the same length predominate. Fig. 2 is a tracing taken of Case I while the ventricular rhythm was irregular and shows five perfectly regular beats in succession with shorter and longer beats coming before and after them. This same patient previously showed a perfectly regular ventricular rhythm for several days. It is difficult to explain the regular rhythm as due to an idioventricular mechanism and then maintain that the tracing shown in Fig. 2, which has so many regular beats, is due to the customary partial block that always accompanies auricular fibrillation. Is it not possible that in both instances we are dealing with a partial block which at one time is varying and at the others constant?

Conclusions. Regular ventricular rhythm with a rate over 55 per minute occurred under digitalis treatment as a transient phenomenon is about 2 per cent of 614 cases of auricular fibrillation. Attempts were made unsuccessfully in 3 cases to vary the ventricular rate by vagal stimulation or vagal inhibition (atropin). There is no proof that this mechanism is due to constant partial

block similar to that of regular ventricular rhythm in auricular flutter, although this remains a possibility. There seems to be definite evidence that digitalis in many cases accelerates the dissociated ventricle.

BIBLIOGRAPHY.

1. Lewis, Thomas: Heart, 1912, **3**, 279.
2. Mackenzie, J.: British Med. Jour., 1911, **2**, 872.
3. Lewis, Thomas: Mechanism of the Heart-beat, Paul Hoeber, New York, 1920, p. 306.
4. Gerhardt, D.: Zentralbl. f. Herzkrankh., 1910, **2**, 339, 373.
5. Cohn, A. E., and Lewis, Thomas: Heart, 1912, **4**, 15.
6. Falconer, A. W., and Dean, J.: Heart, 1912, **3**, 247, and **4**, 87.
7. Freund, H.: Deutsch. Arch. f. klin. Med., 1912, **106**, 1.
8. Edens, E., and Huber, J. E.: Deutsch. Arch. f. klin. Med., 1916, **118**, 476.
9. Kahn, R. H.: Zentralbl. f. Herzkrankh., 1910, **4**, 361.
10. Taussig, A. E.: Arch. Int. Med., 1912, **11**, 355.
11. Neuhof, S.: Am. Jour. Med. Sci., 1923, **165**, 34.
12. Lewis, Thomas, Feil, H. S., and Stroud, W. D.: Heart, 1920, **7**, 191.
13. Lewis, T., Drury, A. N., Bulger, H. A., and Iliescu, C. C.: Heart, 1920, **8**, 83.
14. Hewlett, A. W.: Heart, 1923, **10**, 9.

RIGHT DIAPHRAGMATIC HERNIA OF THE SHORT ESOPHAGUS TYPE.

By Solomon Fineman, M.D.,

FELLOW IN MEDICINE, THE MAYO FOUNDATION,

AND

H. Milton Conner, M.D.,

SECTION ON MEDICINE, MAYO CLINIC, ROCHESTER, MINNESOTA.

At the Mayo Clinic the incidence of diaphragmatic hernia has been 1 in 23,000. We find in the literature reports of 5 cases of para-esophageal diaphragmatic hernia, in which the esophagus was also shortened congenitally. Our case is probably of the same type, and we report it because of the rarity of the condition and because we wish to call attention to the fact, hitherto not mentioned, that this type of hernia is irreducible surgically.

Cases Reported in the Literature. Dietlen and Knierim's[1] patient was a woman, aged twenty-four years, who complained of pain in the right chest, occurring shortly after eating. A roentgenogram revealed a shadow in the right chest, which was interpreted as fluid, but aspiration failed to reveal the presence of fluid. On subsequent roentgenological studies a right diaphragmatic hernia of the stomach of the short esophagus type was found.

Bund's[2] case of diaphragmatic hernia occurred in a male child aged eight months. The diagnosis was established at necropsy. A tumor of the posterior portion of the mediastinal pleura was found extending into the cavity of the right chest. The tumor

proved to be a hernial sac, containing the entire fundus and two-thirds of the body of the stomach, which had herniated through the hiatus of the esophagus. The pyloric end of the stomach protruded through this hiatus and lay beneath the lower surface of the liver. The esophagus lay directly behind the trachea and descended as far as the bifurcation of the trachea, coursed slightly to the right, then suddenly turned to the right and entered the hernial sac from above (Fig. 1).

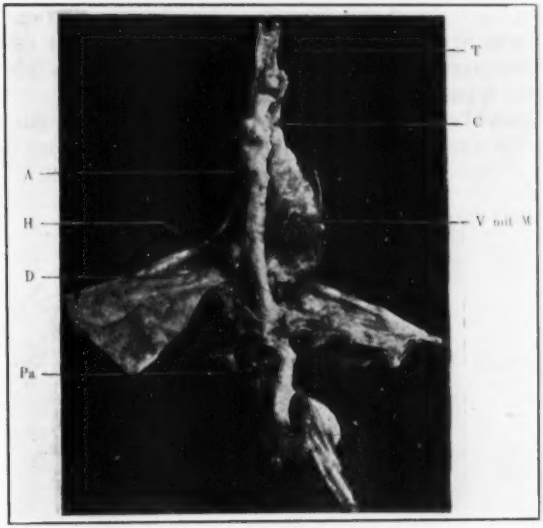


FIG. 1.—Bund's case. Note short length of esophagus at its entrance into the uppermost portion of stomach at C which lies practically entirely above the diaphragm D.

Plenck's[3] patient was a man, aged forty-four years, who complained of a "delicate stomach," which had caused him considerable distress practically all his life. He had had several roentgenological examinations and a diagnosis of right diaphragmatic eventration had been made. He was finally operated on because of evidence of perforation and peritonitis; a right para-esophageal diaphragmatic hernia of the stomach was found. The duodenum was drawn vertically up against the esophageal foramen, and the contents of the stomach were seen exuding from the esophageal hiatus. All attempts at reduction proved futile. The author explains his failure to reduce the stomach on the basis of numerous adhesions and an inability to prolong the operation in view of the patient's critical condition. Death ensued in nine days. Necropsy revealed a shortened esophagus and abnormal position of the stomach, the major portion lying in the right chest. There was a

perforated gastric ulcer 3 cm. above the hernial ring. The esophageal hiatus formed the hernial aperture. The stomach was lying in the chest, with its greater curvature to the right and the lesser curvature to the left. The esophagus entered the stomach at the level of the ninth dorsal vertebra and measured 19.5 cm. from the cricoid cartilage. The average normal length of the esophagus is from 23 to 25 cm.

Huffman[6] found the condition at the dissecting table. No data were obtainable except that the patient had died with symptoms indicating myocardial insufficiency. The greater portion of the stomach was in the posterior mediastinum, the pyloric end being in the esophageal hiatus. The esophagus ended 3 cm. above the esophageal hiatus.

In Tonndorf's[7] case, observed at necropsy, the esophagus did not reach to the esophageal hiatus, and was 4 to 5 cm. shorter than the average. This man died at the age of seventy-six years.

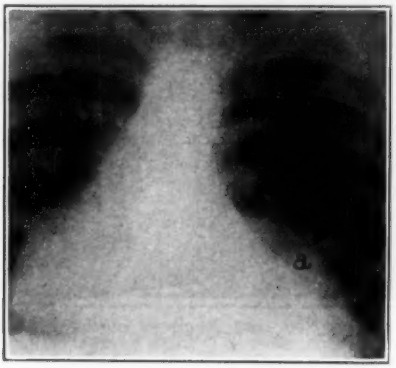


FIG. 2.—Shadow at *a* above right diaphragm, mistaken at first for "encysted fluid" in chest.

REPORT OF A CASE OBSERVED AT THE MAYO CLINIC. **Case History.** (A380336.) J. H., aged twenty-two years, a painter, came to the Clinic because of marked pallor and palpitation. He had had these symptoms intermittently for many years, with periods of well-being between attacks. He had seen many physicians and had been treated for the past seven years for pernicious anemia. There was no history of gastric disturbance.

On physical examination the salient findings were marked anemia and a somewhat enlarged cardiac outline, over which systolic and diastolic murmurs were heard. A shadow above the right diaphragm was revealed by the roentgenogram (Fig. 2), which was interpreted as encysted fluid. We were unable to elicit physical signs to account for this shadow. The patient was admitted to hos-

pital and transfused. His general condition and anemia were improved considerably; the cardiac murmurs disappeared, but a roentgenograph again showed the previously noted shadow. Diaphragmatic hernia was suspected, and a roentgenological examination confirmed the

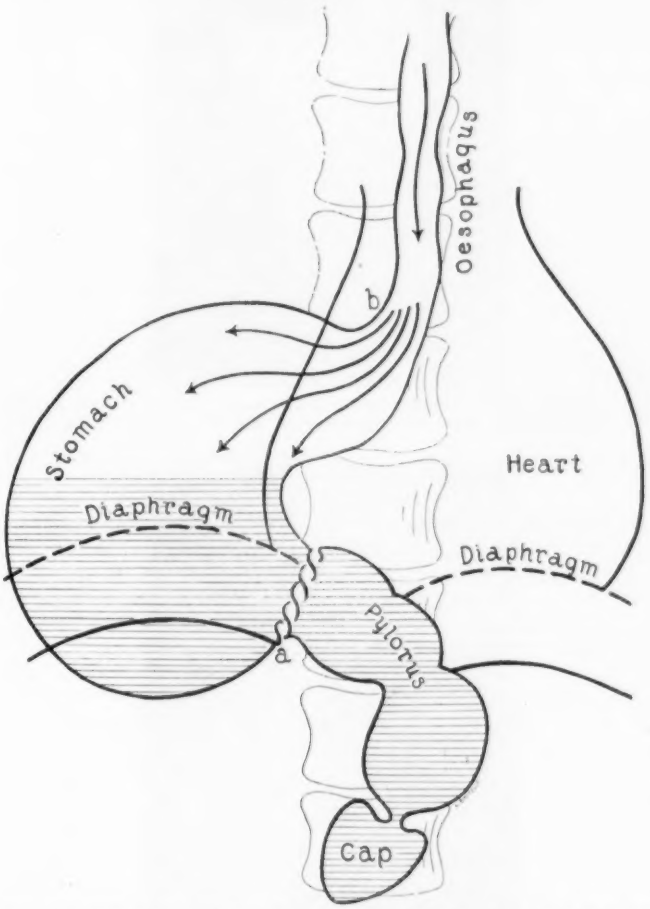


FIG. 3.—Diagram of esophagus, stomach and diaphragm. Note hernial opening in diaphragm at *a* and entrance of the shortened esophagus into the uppermost portion of the herniated stomach at *b*.

diagnosis. The esophagus was seen to descend on the left of the spinal column (Fig. 3), about three-quarters of the way down to the diaphragm. It then crossed the midline abruptly to the right and entered at a point well above the diaphragm into a pouch

lying in the right chest posteriorly. The passage of the bariumized meal failed to demonstrate any sharp kinking or blocking of the

FIG. 4.—Postero-anterior roentgenogram taken in upright position showing herniated stomach in right chest. Note gastric rugæ at *a*. Compare with Fig. 1.

FIG. 5.—Anteroposterior roentgenogram, taken lying down, showing non-filling pressure defect in stomach at *a* caused by the diaphragmatic hernial ring. Note reversed position of greater and lesser curvatures, and absence of distortion or kinking of fundus and cardia at *b*.

esophagus. The barium mixture propelled by esophageal peristalsis emptied into the supradiaphragmatic portion of the stomach

in the form of an intermittent fan-shaped spray. The usual gastric bubble and gastric rugæ were visualized fluoroscopically

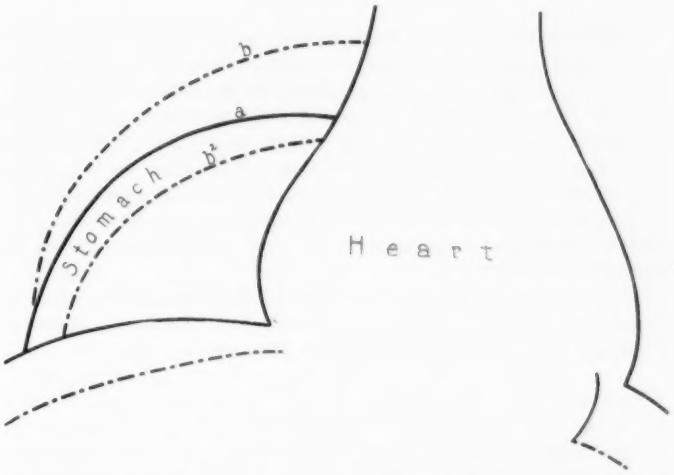


FIG. 6.—Fluroscopical tracing of stomach at rest at *a*, and on full expiration, *b*, and inspiration, after administration of Seidlitz powder, b^2.

and roentgenographically (Fig. 4). The opaque medium was then seen to pass through a diaphragmatic opening (Fig. 5) located posteriorly and practically in the midline into the pylorus which was lying below the diaphragm. The duodenum was normal. The

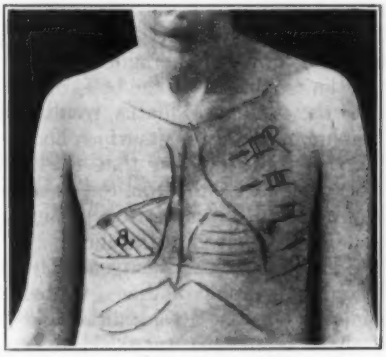


FIG. 7.—Percussion outline of tympanic area *a* corresponding to supradiaphragmatic portion of stomach after administration of Seidlitz powders.

diaphragmatic leaves moved normally, synchronously and freely. At a subsequent fluoroscopic examination the administration of

Seidlitz powder was seen to cause a moderate dilatation of the herniated portion of the stomach (Fig. 6). The outline of the gas-distended stomach could be percussed with some degree of accuracy (Fig. 7).

Using the kymographic method of Hardt and Joseph[4] for the study of intragastric tension, it was determined that on inspiration and expiration the tension variations in the supradiaphragmatic stomach were the reverse of what is usually found in the normal stomach. With inspiration and expansion of the thoracic cage there was a fall in intragastric tension. With expiration and contraction of the thoracic cage there was a rise in intragastric tension. In this experiment no difficulty was experienced in passing a tube into the stomach. Free hydrochloric acid was demonstrated in the aspirated contents.

No operative procedures were attempted. This patient has been heard from recently, two years after his first examination, and he is not having symptoms referable to the hernia.

Embryology. Broman[5] has shown that, in the human embryo, the lesser peritoneal cavity encircling the intestine is constricted by the fusion of the diaphragmatic anlagen, with the consequent formation of a blind sac, bounded on the left by the right mesodermal wall of the esophagus, on the right by the diaphragmatic anlage, and in part also by the right lung. In certain persons this bursa quickly disappears; in others, however, it enlarges and may often be found in the adult as a slit about 1 cm. or more in diameter, between the esophagus and right leaf of the diaphragm.

Bund[2] is of the opinion that a malunion of the diaphragmatic anlagen results in the persistence of a communicating canal between the lesser peritoneal cavity and the infracardiac bursa. In the presence of such a communication abdominal organs enter the infracardiac bursa and form a diaphragmatic hernia. He explains the shortening of the esophagus on the basis of a deficient fixation of its distal end to the esophageal hiatus, resulting from maldevelopment of the diaphragmatic segments which bound the esophageal opening. Plenck[3] is of the opinion that the shortening of the esophagus can be explained either on the basis of a congenital hypoplasia, or by a lack of normal growth stimulant, due to the abnormal position of the stomach in the chest.

Discussion. On the basis of the roentgenologic findings, in part confirmed by the kymographic findings, we believe that we are justified in considering our case a congenital right para-esophageal hernia, of the short esophagus type. However, whether this particular case is or is not of this type, the fact remains that such hernias have been proved to exist, and that in 1 case an attempt at surgical reduction was made. In reviewing the literature on diaphragmatic hernia we find no mention of the fact that a com-

plete reduction of the stomach from the chest into the abdomen is impossible because of the congenitally shortened esophagus. It seems essential, for the sake of intelligent management, that every patient with diaphragmatic hernia of the stomach should have a careful roentgenologic examination with the specific object in mind of determining, so far as possible, the length of the esophagus.

Summary. The incidence of diaphragmatic hernia at the Mayo Clinic is 1 in 23,000 cases. The case of diaphragmatic hernia reported was on the right side, and in all probability of the short esophagus type. The intragastric tension in this case was found to be the reverse of what is usually found in a normal person. In such hernias, on account of the congenitally shortened esophagus, we believe complete reduction of the stomach from the chest into the abdominal cavity is impossible. Therefore, for the sake of rational management, every patient with diaphragmatic hernia involving the stomach should have a careful roentgenologic examination with the specific object in mind of determining, so far as possible, the length of the esophagus.

BIBLIOGRAPHY.

1. Dietlen, H., and Knierim, G.: Hernia diaphragmatica dextra, Berl. klin. Wchnschr., 1910, **1**, 1174–1177.
2. Bund, R.: Ein Fall von rechtsseitiger Hernia diaphragmatica mit Austritt des Magens in den persistierenden Rezessus pneumatoentericus dexter, Frankfurter Ztschr. f. Path., 1918, **21**, 243–257.
3. Plenck, A.: Zur Kazuistik der Zwerchfellhernien, Wien. klin. Wchnschr., 1922, **35**, 339–341.
4. Hardt, L. L. J., and Joseph, E. G.: Kymographic Studies of Various Pathologic Conditions of the Stomach, Med. Clin. North America, 1923, **7**, 63–79.
5. Broman, I.: Normale und abnorme Entwickelung des Menschen, Wiesbaden, J. F. Bergman, 1911, pp. 828.
6. Huffman, L. F.: A Case of Diaphragmatic Hernia Observed at Postmortem. Ann. Surg., 1920, **72**, 665–667.
7. Tonndorf, W.: Wahre Zwerchfellhernien als Folge einer Wachstumshemmung der Speiseröhre, Deutsch. Ztschr. f. Chir., 1923, **179**, 259–265.

THE HYPOPHYSEOBASAL AREA IN ITS RELATION TO THE PATHOGENESIS AND TREATMENT OF DIABETES INSIPIDUS AND POLYURIA.

(Including a Study of Thirty Autopsies)

By Charles E. de M. Sajous, M.D., LL.D., Sc.D.

Professor of Applied Endocrinology, University of Pennsylvania Graduate School of Medicine, Philadelphia.

In the issue of the American Journal of the Medical Sciences for November, 1922, I submitted that despite prolonged researches, the physiologists had been unable so far to point out the actual

function of any ductless gland and that this was due to the fact that the true role of these organs could only be discerned by a concomitant analytic and synthetic study of all branches of medical science bearing directly or indirectly upon the subject studied. Suggestive in this connection is a recent critical examination of the current views concerning the internal secretions by Prof. Swale Vincent[1] of the University of London, in which this physiologist emphasizes the need of a "reconsideration of our whole attitude in relation to the pituitary body." In keeping with this conclusion, it may be recalled that for over two decades, I have urged that the prevailing views concerning this organ were erroneous.

The particular labors to which Vincent refers are those of two French internists, Camus and Roussy (1913 and 1920),[2] and of Bailey and Bremer (1921).[3] Camus and Roussy denied that polyuria was due to lesions of the hypophysis. They had observed intense polyuria after hypophysectomies in dogs, but careful necropsies showed that this occurred only when the basal tissues had been injured. When the hypophysis was removed alone without such injury, polyuria failed to appear; when, however, the basal tissues were injured and the hypophysis was left intact, polyuria occurred invariably. Their numerous experiments showed that the question of depth of injury in the basal tissues was of no moment; a superficial lesion sufficed provided it was located "at the level of the gray substance of the *tuber cinereum* in the vicinity of the infundibulum." Bailey and Bremer[4] also found, in 13 adult dogs, that even an extremely minute lesion in the same area, *i. e.*, the parainfundibular region of the hypothalamus, invariably caused polyuria within two days, its duration depending upon the extent of the lesion and varying from six days to apparent permanence. It possessed all the characteristics of human diabetes insipidus. They found that an extensive lesion of the tuber cinereum was incompatible with life, the animals dying rapidly or after a period of apathy, in coma and convulsions. The integrity of the hypophysis was verified histologically in each case, thus eliminating this organ as a cause of the experimental polyuria induced.

Similar results were obtained by Houssay and Hug.[5] They found that animals deprived of the hypophysis excrete the same amount of urine as the controls, and that where the animals drank water, the diuresis was actually less than in the controls. Houssay[6] also denies that polyuria is due to hypersecretory activity of the hypophysis. His experiments showed that it was produced by lesions of the cerebral basal zone similar to that first defined by Camus and Roussy in 1913. He is inclined to believe, however, that the posterior lobe may structurally participate in the pathogenic process.

Indeed, to eliminate the posterior lobe from the pathogenesis of diabetes insipidus or polyuria introduces many difficulties. As shown by Falta, Marañon and others, compression of the median

and posterior lobes by an enlarged anterior lobe will also produce diabetes insipidus. Quite in keeping with this clinical and experimental fact is the polyuria of pregnancy in which, as is well known, the anterior lobe is enlarged and must, therefore, compress the posterior. But there is no involvement of the basal tissues here. As shown by Cyon, Masay and others, the slightest touch upon the exposed pituitary will produce a marked rise of blood-pressure while slight electrical stimulation will do likewise. Cushing[7] observed also that mere manipulation of the posterior lobe sufficed to cause diuresis in experimental animals and sometimes intense and prolonged polyuria. Yet, while compression may cause it, Cushing likewise found that the opposite, sellar decompression by surgical measures addressed to the anterior lobe thus preventing pressure from the posterior lobe, brought on a severe polyuria—a result also noted in one of my cases. Again, if this identical lobe be disconnected from the basal tissues either experimentally as observed by Cushing and others, or accidentally as in the case of a boy shot in the head observed by Marañon and Rosique,[8] prolonged polyuria is also produced.

Nor can we attribute any of these phenomena to a hypophyseal secretion. Not only can they all be produced, we have seen, by lesions above the hypophysis, and far away from it as we shall see, but injections of fluid from the cerebrospinal canal thought by Cushing and Goetsch to contain the specific hypophyseal secretion proved inert in polyuria, as shown by Houssay and Roman,[9] Marañon,[10] and Dixon and Cow,[11] where pituitary preparations proved active. An extract of choroid plexus, also thought by Weed and Cushing to secrete a pressor substance into the fourth ventricle fluid, was likewise tried by Dixon and Cow in polyuria but found inert, while hypophyseal extract at once produced its typical effects. In a comprehensive investigation of the subject, Jacobson[12] found "no definite evidence of the presence of a pressor substance in the cerebrospinal fluid suggestive of any posterior lobe secretion." Indeed, the bulk of present day evidence clearly indicates that, as stated by Souques, Alajouanine and Lermoyez[13] at the recent Third International Congress of Neurology, posterior lobe preparations do not represent a secretion of this organ but only pharmacological products.

This is the view that I have urged many years, the effects of these products being at the time attributed mainly to adrenin, as first pointed out by Howell. The tissues of the posterior lobe not only give the chromophile test and other adrenalin color tests, as observed by Watanabe and Crawford,[14] but they also raise the temperature, according to Rogers,[15] and likewise the basal metabolic rate as recorded by McKinlay[16]—all phenomena which injections of adrenalin likewise provoke. Clinical experience has also shown that the effects of posterior lobe preparations are similar to those of adrenal

preparations, though more prolonged, owing to the presence of constituents resembling those of the cerebral cortex.*

The Hypophyseorenal Path. The pathogenesis of diabetes insipidus and polyuria no longer stands in the present inexplicable position, however, when, as its embryological origin indicates, the posterior lobe is regarded as a neural structure, and, as I first urged in 1908,[18] *as the starting point of several sympathetic paths one of which extends via the tuber cinereum, the bulb, cord and splanchnic nerves and renal plexus to the vessels of the kidneys.*†

It is important to bear in mind in this connection, that there exists at the base of the brain a nuclear aggregate which can carry on all vegetative or somatic functions quite independently of the cerebral hemispheres proper. Its efficiency as such was amply demonstrated by Wilbur's frog, which lived five years after removal of its cerebral hemispheres, Goltz's dog, which lived eighteen months after the same procedure, including destruction of the optic thalami, and which even refused food made bitter with quinine, and Vulpian's demonstration that removal of the hemispheres, optic thalami, striated bodies, corpora quadrigemina and the cerebellum did not prevent the animals from crying out when an exposed nerve of its foot was pinched. Nor does removal of the both hemispheres from a pigeon prevent it from shaking off a fly that happens to alight on its head. So conservative a physiologist as Sir Michael Foster[19] referring to such animals, wrote that "they may be kept alive and in good health for a long time" and that they exhibit "a spontaneity obviously betokening the possession, not merely of a conscious volition, but a certain amount of intelligence."

From my viewpoint, however, sustained by much accumulated evidence, the posterior or neural lobe of the pituitary, in keeping with its identity as an extension downward of the neural ectoderm which eventually becomes the floor of the third ventricle, forms part of the basal aggregate of nuclei to which Foster refers. I regard it in fact as forming *an individual mechanism similar to one of the cerebral motor areas, which I would term the hypophyseobasal area.*" Indeed, a careful analysis of this lobe by MacArthur[20] showed that "the chemical composition of the hypophysis resembled the gray matter or young nervous tissue in most respects" . . . "In

* This conclusion is not modified by the recent observation of Dixon,[17] that pituitary extract injected into the cerebrospinal fluid or into the circulation caused the pituitary to secrete. That a balance was struck between the amount in the blood and the cerebrospinal fluid indicates mere diffusion, while the fact that the latter fluid gave the chemical and physiological reaction of pituitrin is but a normal outcome when the posterior pituitary is considered as a nervous structure, since both fluids would contain the same neural constituents. From my viewpoint the actual participation of a pituitary "secretion" in the process is only assumed.

† The term "path" employed here is intended merely to denote a nervous connection between the hypophyseobasal area and the kidney, the true identity of which is still to be determined. There are a number of descending tracts concerning which our anatomical knowledge is still obscure.

those respects in which the two lobes differ the posterior is more like the gray matter than the anterior," a fact which various his-

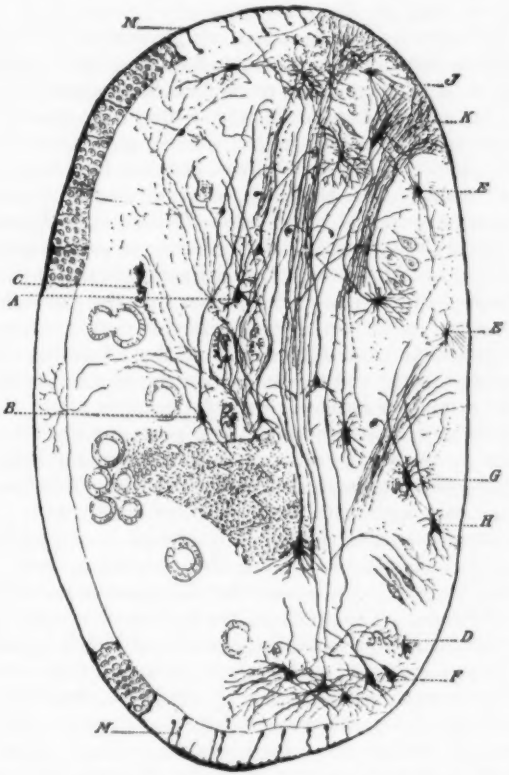


FIG. 1.—Vertical section of the neural lobe of the hypophysis. (Berkley.) Schematic, to illustrate the various types of cells in the 2000 sections of this lobe examined. *M*, outer layer over posterior surface of lobe, composed of gray matter (Luschka, Müller), and ball-tipped ependymal cells; *A*, widely distributed cells with many ramifications; *B*, similar cells, centrally located with long upward, brush-tipped processes; *C*, centrally located cells, resembling closed follicles, with comb-like tufts; *D*, neuroglia cells; *E*, spider cells in large quantities similar to, but larger than, those in cerebral tissues; *F*, ganglion cells which traverse entire organ upward and end in infundibular area; *G*, large pyramidal cells; *H*, pyramidal cells with short dendrites; *J* and *K*, ramifications of long dendrites, tufted figures and feathery protoplasmic cells, also cells covered with thorns which give off strong dendrites. These cells are not found elsewhere in the nervous system and occur in the upper border of the neural lobe "along the space *formerly* occupied by the infundibular duct."

tologists had also observed. Luschka,[21] Müller[22] and others who studied the hypophysis from myxine to man found that its gray matter extended upward along the infundibulum up to and including

the floor of the third ventricle. So marked were these histological characteristics, coupled with many facts, biological, physiological and clinical, recorded and personal histological studies, that I ventured in 1907 to term the hypophysis—including the basal nuclei—the *somatic brain* to convey its physical limitation to body or vegetative functions, as distinguished from the *psychic brain*, the organ of mind, the pallium or cerebral hemispheres overlying it.

There can be no doubt regarding the identity of the posterior lobe of the hypophysis as a nervous organ. In keeping with embryological and morphological data which have caused it to be termed by anatomists the "neural lobe," Berkley[23] found histologically that it contained numerous typical nerve cells. Osborne and Vincent[24] and other observers have likewise described true nerve cells and fibers in the posterior lobe. Moreover, knowledge gained in recent years on the histochemistry of the lipoids has shown that the glia cells claimed to be alone present by the opponents of this view, are composed of phospholipoids and cholesterin similar to those found in the myelin of the nerves at large and the brain. In the illustration of the posterior lobe submitted herewith, one of Berkley's plates, this organ is shown to contain a close and thick plexus of fine fibers which ramify among the nerve cells, constituting "terminal arborizations of a bundle which passes downward in the infundibulum," while other fibers pass upward to the basal tuber cinereum.*

As to the relations of the hypophysis with the basal tissues by nerve paths, Cajal found that the fibers passed up mainly to the giant-celled nucleus in the basal tuber cinereum immediately above the infundibulum. This nucleus, the largest of a series of paired ganglia, was described by both Lenhossek and Kölliker, and termed by the latter histologist, *nuclei tuberii*, owing to their situation in the *tuber cinereum*. This region in turn was described by Sir Michael Foster as "*a continuation of the spinal gray matter.*"

Authors who refer to the infundibulum as a canal through which a secretion is supposed to pass up to the third ventricle, overlook the fact recalled by Piersol[25] that, while "in the very young child the infundibulum retains to some extent its original character as a hollow outgrowth from the ventricle, in the mature subject this cavity, the recessus infundibuli, has mostly disappeared and the stalk is solid save for a slight diverticulum within its upper and widest path," thus affording a path for the nerve fibers to the basal tissues. As shown in the illustration herewith (*J* in the descriptive text) long dendrites are present "in the space formerly occupied by the infundibular duct."

* The remarkable activity of hypophysis sicca and pituitrin, both posterior lobe preparations, bespeaks the presence in this lobe of a rich supply of nuclear materials besides adrenin. This in itself stamps as misleading the often-published statement that the neural lobe contains but a few neuroglia cells and degenerated nervous tissue, that it is but a vestigial organ, and so forth.

That the hypophysis influences the body at large, including the brain, has been noted by various physiologists. De Cyon[26] and also Masay[27] found, we have seen, that the slightest touch of the organ through an opening in the sella turcica, and only after the animals had entirely recovered from the operation, produced a marked rise of blood-pressure and reduced the heart beats. Pirrone[28] thought he disproved these observations because he found that stimulation of the basal tissues above the hypophysis produced the same effects as those observed by de Cyon and Masay. But he only confirmed their views as to the peripheral effects described, and also my own (1903)[29] that it is through nerve paths *beginning* in the hypophysis and passing through the tuber cinereum via its nuclei that these vasomotor effects were evoked. Weed, Cushing and Jacobson[30] also found that faradization of the pituitary gave rise to glycosuria, a fact clearly explained by the effect of impulses through a path from the same organ to the adrenals which I have described elsewhere.[31] Finally, I might also recall the observation of Schäfer[32] that experimental injury of the hypophysis gave rise to polyuria, a result due to impairment of the hypophyseorenal nerve-path previously referred to as having been first described by myself in 1908[18] and the existence of which will now be further sustained.

Diabetes Insipidus Due to Lesions along the Hypophyseorenal Path. The need of such a path to explain the pathogenesis of diabetes insipidus was shown by a personal study of thirty and odd unselected cases reported in the literature of the lasty thirty-eight years. These necropsies clearly show by lesions situated all along the hypophysiorenal path extending from the hypophysis *per se* to the kidneys, that this one disease—or symptom of many local pathological processes—diabetes insipidus, can be produced by impairing the functions of this path *anywhere throughout its course*.

Lesions of the Posterior Lobe per se. Twelve of the recorded cases showed that the neural lobe alone could be the seat of various kinds of local processes capable of causing diabetes insipidus. Benario[33] described a case in which a gumma was found in this lobe at autopsy. Two similar observations have been recorded by Sequeira[34] and Berge and Schulmann,[35] Marañon[36] also refers to cases reported by Spanhock and Goldzeiher. Metastatic cancer of the posterior lobe was found by Simmonds[37] in 3 cases with intractable polyuria. In 1 similar case recorded by Neuburger,[38] and in 2 reported by Sekiguchi,[39] all 3 showed marked polyuria; [the basal gray matter was also examined and found to be the seat of no pathological changes.

Lesions in Both Lobes or in the Infundibulum. Six of this class were recorded. In a case of diabetes insipidus autopsied by von Meyenburg,[40] a cancerous process included both the middle and posterior lobes. Cushing observed a case in which metastatic lymphosarcoma of the infundibulum was found postmortem. In a

case of teratoid cyst recorded by Globus and Strauss,[41] both lobes and the infundibulum were compressed. In one reported by Newmark,[42] the posterior lobe and nearly all the pars intermedia were also found destroyed. Luzzatto[43] observed a case of polyuria in which autopsy showed that destructive hemorrhage of the posterior lobe had separated the latter from the infundibulum. In another reported by Chauffard,[44] a fungous tumor had destroyed the hypophysis without involving the basal tissues.

Lesions of the Infundibulum and Tuber Cinereum. Two cases had been recorded in which the diabetes insipidus was due to lesions involving the nerve path in these areas. In one reported by Römer[45] the disease proved at autopsy to have been due to a tumor involving both the posterior lobe and the overlying basal tissues; in one observed by Lhermitte,[46] a syphilitic lesion was found to involve both the infundibulum and the tuber cinereum. That puncture of the latter produces polyuria is recalled by Veil.[47] Also emphasizing this fact, Leschke[48] states that bullet wounds, tumors, gummata, tubercles and other lesions in this location may all produce this condition, without lesion in the hypophysis proper, in accord with the observations previously submitted.

Lesions in the Bulb. Seven cases of this class examined post-mortem were found. Lecorché and Talamon[49] over thirty years ago urged the importance of syphilitic sclerogummatous lesions in the neighborhood of the floor of the fourth ventricle as a cause of diabetes insipidus and reports 2 cases in which nervous phenomena due to irritation of local nerve paths occurred. Ebstein,[50] in 6 cases of diabetes insipidus due to syphilis, found lesions in the medulla oblongata in 3. Marinesco[51] reported a case in which the autopsy showed a gliosarcoma in the floor of the fourth ventricle. Even edema in this region as observed by Weiszbarth[52] may cause diabetes insipidus. I might recall in this connection that as shown by Bernard, a *piqûre* very near to that which causes glycosuria will cause polyuria; also that *piqûre* of the tuber cinereum produces the latter; and, finally, that diabetes mellitus and diabetes insipidus often occur together.

Lesions of the Spinal Cord and Splanchnic Nerves. That diseases of the spinal cord—which in the present connection would involve the hypophyseorenal path—sometimes show diabetes insipidus as a complication is well known. Futcher[53] refers to a case of tabes seen by Schlesinger; to one of spastic paralysis reported by Westphal; to one of diffuse tumor of the cord observed by Shultze; to some of syringomyelia seen by Krause, and of hereditary ataxia reported by Friedreich in which polyuria was more or less persistent. As to the paths from the cord, "cases of diabetes insipidus are also recorded," writes Eichhorn,[54] "in which degenerative changes have been found in the sympathetic system, notably in the coeliac plexus and the great splanchnic nerves." These, as is well known, form,

with renal branches of the lesser splanchnic, the renal plexus which supplies nerves to the renal arteries.

A connection with the hypophysis has also been urged recently (1916) by Motzfeldt,[55] of Christiania, who, after a critical study concluded that "although the disease is comparatively rare, a number of cases had been recorded during recent years" (to which the autopsied cases I have quoted above may be added) in which "their connection with the hypophysis has been proved beyond a doubt" . . . "The posterior lobe of the hypophysis seems to exert a constant physiological influence on renal functions."

How are the kidneys influenced by the hypophyseorenal path through the splanchnic by stimulation and diuretics? I may recall in this connection that in 1908[18] I submitted that "when the flow of urine is to be increased, the renal arterioles are dilated by vasodilator terminals of the sympathetic which reach the organ by way of the splanchnic nerves and the semilunar ganglia. The glomerular tufts being thus traversed by a greater volume of blood, the components of urine are thus filtered out into Bowman's capsule." That increased cellular activity, through vasodilation with congestion, as first taught by Bernard, is one of the main features of active diuresis and of diabetes insipidus is emphasized by its pathology. "The only thing that can positively be stated," says Futcher[56] in reference to this disease, "is that it is due to some nervous influence causing a vasomotor disturbance of the renal vessels, leading to persistent congestion of the kidneys. The only constant finding at autopsy is enlargement and congestion of the kidneys."

On the whole, the foregoing data tend to show that diabetes insipidus can be produced when any condition, gumma, tuberculoma, cancer, focal hemorrhage, cicatricial tissue, etc., located in or involving either the posterior lobe, the infundibulum, the overlying tuber cinereum, or any of these structures jointy, or any other portion of the hypophyseorenal path, sufficiently interferes with the transmission of its impulses to the renal vascular system to allow too great a volume of arterial blood to traverse the organ and its secretory elements.

Besides causative lesions in the hypophyseorenal nerve-path, however, there are various disorders which induce diabetes insipidus or intense polyuria by acting upon this path in other ways.

Diabetes Insipidus and Polyuria Due to Compression of the Hypophysis and its Basal Nerve Paths. Pregnancy is a familiar cause of diabetes insipidus. Though a physiological process, it is well known that the anterior lobe becomes enlarged. In the light of the foregoing facts this is due to the pressure exerted upon the nervous elements of the posterior lobe, the osseous posterior wall of the sella affording the necessary resistance, which pressure interferes with the functions of the organ's nuclei, and inhibits the formation of the

impulses to the kidneys. All this applies also to acromegaly, which often includes diabetes insipidus in its symptom-complex. The polyuria may be either temporary, as is often the case in pregnancy, or if microscopical lesions develop in the hypophysis as a result of the pressure, it may last indefinitely. Hypophyseal tumors are also known to cause diabetes insipidus. We thus have a series of factors capable of evoking this symptom and which if located in the anterior lobe can compress posteriorly the pars intermedia and the posterior lobe and thus inhibit more or less the functions of the latter. It would be difficult to prove that the basal tissues are invariably involved in the pathogenic process of such cases otherwise than as a conducting path.

Ample evidence also attests, however, the causative influence of pressure from disorders in structures external to the hypophyseobasal area. In a case observed by Lépine,[57] for instance, the autopsy showed a tumor of the optic thalamus, immediately above, therefore, the tuber cinereum. The polyuria had appeared suddenly and the large size of the tumor indicated that it compressed the latter and probably, as Lépine thought, "the pedicle of the hypophysis."

In this case pressure must clearly have blocked the passage of impulses to the kidneys. A very similar case was recently reported by Ricaldini[58] in which infantilism of the hypophyseal type was present together with diabetes insipidus. At autopsy a sarcoma was found between the optic thalamus and the tuber cinereum. The latter itself, the infundibulum, and the hypophysis were found macroscopically normal; microscopically, however, slight hemorrhagic foci and lymphocytic invasion of the posterior lobe, the head, in other words, of the hypophyseorenal path. Suggestive in this connection is the remark of Beck[59] in reference to dystrophia adiposogenitalis, that "when associated with tumors in the neighborhood of the hypophysis, especially those involving the chiasm and subthalamic region or with basilar syphilitic meningitis, a true diabetes insipidus may develop." Even fluid compression may cause it. The acqueduct of Sylvius being very small, inflammatory or neoplastic disorders in its neighborhood may readily close it and cause sufficient retention of cerebrospinal fluid in the third ventricle to produce marked pressure upon the nuclei and nerve paths in the tuber cinereum. The pressure may even be exerted from below the hypophysis, as in a case reported by Hamilton[60] in which the cause of the diabetes was found at postmortem to be a tumor of the circle of Willis.

The polyuria of encephalitis lethargica is probably due to a similar process. Such cases have been reported by Briand and Rouquier,[61] Gosset and Gutmann[62] and Bénard.[63] The neural lobe of the hypophysis was first associated with normal sleep by myself (1903),[64] then by Salmon (1905)[65] and others. Bénard, by administering injections of fluid extract of pituitary reduced the polyuria markedly.

so to say at will, the effect lasting only as long as the remedy was used, about twelve hours. A single injection only caused a reduction of the polyuria in twenty-four hours from 19 liters to 5.8 liters. Bénard attributes the intense polyuria to involvement of the hypophysis and the overlying tissues. Pressure by the cerebrospinal fluid in the third ventricle upon the tuber cinereum not only affords a foundation for this interpretation, but the familiar beneficial effects of lumbar puncture in all forms of meningitis is supplemented in the present instance by the fact, first shown by Herrick and confirmed by Cammidge,[66] Tucker[67] and others, that lumbar puncture may also prove beneficial and even curative in diabetes insipidus.

Epidemic encephalitis was attended by diabetes insipidus in a case recently reported by Hall.[68] Some lesion other than the epidemic encephalitis caused pressure upon the tuber cinereum, for there were ocular symptoms, unilateral facial paresis, while the patient was a mental defective. The presence of such a lesion, probably a tumor below and behind the optic thalamus (the sella turcica then showing no roentgen-ray change, as specified) was indeed shown by the return of the patient two years later with marked diabetes insipidus. But neither adrenalin or pituitrin appeared to reduce the urine output, although the latter preparation caused a rise of blood-pressure and relieved the extreme thirst. The renal vascular paresis was so complete in this case that the vasoconstrictor action of the pituitrin could not manifest itself in the kidneys though active throughout the body at large.

Compression from lesions within the hypophysis, or of external origin, upon this organ, the basal tissues or the nerve paths it contains, may thus provoke diabetes insipidus. While the two structures appear capable of causing this symptom separately, the fact remains that a neural path beginning in the hypophysis and passing through the basal tissues seems alone capable of explaining its production. An effort to do so by means of one or more "secretions" soon proves fruitless.

Diabetes Insipidus and Polyuria Due to External Traumatisms; Emotional Stress, Etc. Falls upon the head, concussions, basal skull fractures, fright, etc., have long been accepted as causes of diabetes insipidus and also of various pituitary disorders, notably acromegaly, hypopituitarism and the adiposogenital syndrome. Numerous cases of diabetes insipidus are also clearly due to violent emotions. Marañon[69] observed five such patients and refers to instances recorded by Lereboullet, Van der Heijden, and Germani.

The similarity of the posterior or neural lobe of the hypophysis to the cerebral cortex observed by histologists previously referred to, and many other facts which led me many years ago to refer to this lobe, including its nervous connections with the anterior lobe and the overlying basal ganglia in the tuber cinereum, as a somatic brain, also caused me to refer to it as a *sensorium commune* (1903)[70]

upon which fright, shock, anger, etc., could react by jarring its cellular elements. I may recall in this connection the independence of this organ from the overlying psychic brain as illustrated by the decerebrated animals, frog, fowl, dog, etc., previously referred to. Such an animal, in fact, as emphasized by Sir Michael Foster, "is not wanting in what we ordinarily call a 'will.'" Nor would any one deny its manifestations, besides instinctive acts in lower forms devoid of skull or brain, the amphioxus for example, to which low form Andriezen traced the structures which ultimately become the pituitary body.

All this refers as well to sensibility. Any one who has worked with amphioxus, for instance, knows its almost lightning-like response to any external excitement, the gentlest stimulus or fright, despite the absence in this animal of cerebral hemispheres. Even in man, what sensibility the cerebral cortex affords is limited to "tactile discrimination and localization and perhaps of the finer shades of temperature" and that only in the postcentral convolution. Brubaker (1922),[71] who gives these limitations also, refers to Charles K. Mills as stating that "innumerable cases have been reported of lesions of the motor area (the precentral convolution) without the slightest impairment of sensibility;" these included excision of portions of the motor cortex. As to where a cutaneous injury actually reacts, Schäfer[72] referring to decerebrated animals, concludes: "This no doubt lands us in the unsatisfactory position that we are certainly unable to say in what part we are to localize cutaneous sensibility, or even if it is localized at all in the cortex."

The spinal cord at once suggests itself as a factor in any morbid process due to exogenous trauma, but even here we are brought back to the hypophyseobasal area, *i. e.*, the *sensorium commune*, for as Foster states in this connection, "the phenomena presented by animals deprived of their cerebral hemispheres show that this machinery of coördination is supplied by cerebral structures lying *between the cerebral hemispheres above* and *the top of the spinal cord below*."* Referring to this area as the "tegmental region from the bulb upward," he also states that this region through which ascends the fillet is "a probable path of sensations of one kind or another from the body at large."

That this same area and the hypophysis itself are directly concerned with the perception of common sensibility is shown by the frequency with which pain in one region or another is recorded by many investigators in acromegaly. This pain may be localized in the soft tissues of the face and regarded as "neuralgia" or extend over the entire body. Pirie noted shooting pains in combination with paresthesia, tingling and numbness, and he refers to Sternberg as remarking "particularly on the occurrence of pain and paresthesia

* The italics are my own.

as valuable signs for diagnosis in the *early* stages of the disease." In his own pitiful case, Mark[73] distinguishes emphatically what he terms his "faceache" from the characteristic headache of the disease; it was persistent and always occurred on the left side. Cold air greatly aggravated the intensity of this "neuralgia" or "migraine." Suggestive in this connection is the fact that de Cyon[74] found experimentally in a large number of animals that removal of the hypophysis annulled the nasal sensory reflexes, sneezing, etc., but also that all the nerves including the fifth glossopharyngeus "lost their reflex influence." I have submitted considerable evidence elsewhere[75] showing that touch, hearing and taste were also connected with the hypophysis. We have seen that Goltz's decerebrated dog refused food which contained quinine, that a decerebrated pigeon will shake off a fly alighting upon its head, etc.,—all attesting to the presence of a *sensorium commune* distinct from the brain itself, purely autonomic or vegetative in the normal organism.

As to the modes of production of the many peripheral symptoms observed in hypophyseal disorders, acromegaly in particular, paresthesias, pain, photophobia, hyperacousis, tinnitus, conjunctival congestion, catarrhal disorders of the respiratory tract and the Eustachian tubes, bulimia due to passive congestion of the gastric mucosa, congestive lethargy, heat flushes, edema, etc., they are similar to the cause of polyuria, *i. e.*, passive vasodilation in the tissues which are the seat of the symptom. In pain or hyperesthesia, for instance, the cutaneous arterioles are passively congested and their sensory nerve endings, irritated by the excess of blood they receive, convey pain or heat impulses back to the sensorium commune. This means that we must consider the hypophysis capable of receiving sensory and giving out motor impulses. We have seen that such is evidently the case, the inward impulses reaching this organ by way of the median fillet—a decussation from the funiculus gracilis—while the motor impulses are transmitted to the vessels by way of the spinal and sympathetic systems. All the organs and tissues dominated by this hypophyseobasal somatic brain, are functionally active in proportion as the volume of arterial blood which passes through them is great. Its highly differentiated cells preserve the equipoise of this blood supply and it is to variations of activity of the various cellular groups, which differ greatly as shown in the illustration on page 683 that the many different phenomena awakened by the organ are due.

An important fact to bear in mind in this connection is that diabetes insipidus is the maximum expression of exaggerated diuresis. Gradually descending the scale the severity of the symptom from marked polyuria down to copious diuresis, we reach the emotional causes witnessed during excitement, fear—as observed in troops when first led to attack. These are due to temporary relaxation

of the renal vascular channels under the influence of the emotional stress acting centrally upon the hypophyseal sensorium, commune.

Treatment. The treatment of diabetes insipidus was very unsatisfactory and uncertain in its results when Francesco Farini (1913)[76] gave us what constitutes virtually a specific by introducing the use of pituitary extract in hypophyseal polyuria. The posterior lobe fluid preparations given hypodermically in 10 to 15 minim (0.6 to 1 cc) doses, have been found to act very efficiently, not only reducing markedly the polyuria but also the intense thirst. In the light of the views submitted above, the explanation of this result suggests itself: The posterior lobe preparation acts upon the renal arterioles as it acts elsewhere in the body; it promotes their contraction. That this is the result of a pharmacological action was recently shown by Weir, Larson and Rowntree[77] who found that these preparations acted when all the nerves to the kidneys had been severed.

Unfortunately, the action of pituitary preparations is ephemeral and the injections must be administered daily at least to sustain the beneficial effects—two defects which render the method difficult except in hospitals. To obviate them, I used successfully in a very severe case of diabetes insipidus due to pituitary tumor in a child aged twelve years, and which persisted despite a decompression operation, a combination of the hypophysis sicca, $\frac{1}{10}$ gr. (0.006 gm.) and ergotin, 1 gr. (0.06 gm.) in a capsule. This was given orally three times daily, the ergotin being added to reinforce the vasoconstrictor action of the posterior pituitary. The polyuria gradually decreased until the daily output became normal. Up to the time of the present writing, two years after this treatment ceased, the polyuria had not returned. Rees and Olmstead[78] found in one case that by covering the posterior-pituitary preparation used with salol, the effects were as satisfactory as when the hypodermic method was used, provided, however, that in addition to the daily dose, one be administered also at bedtime.

The enuresis of children is also due in some instances to functional adynamia of the hypophyseobasal area. Hence the beneficial effects of posterior lobe preparations in the treatment of many of these cases.

The apparent innocuousness of removal of the posterior or neural lobe recorded by Paulesco, Cushing and others, would seem calculated to offset the deductions submitted. But it only proves anew that this lobe at least is not a secreting organ, since we know that removal of *bona fide* endocrine glands, the thyroid or adrenals, for example, gives rise to marked phenomena. Conversely, as a coördinating center, the neural lobe, from my viewpoint, contributes no hormone to the life process itself, but forms part of a sympathetic nuclear mechanism which regulates the admission of arterial blood to the cellular elements. When we administer preparations of this lobe, therefore, we add to the blood an agent rich in organic phos-

phorus and adrenin which, by reducing the caliber of its arterioles, restores the normal renal circulatory equilibrium and thus prevents the polyuria.

Again, removal of the *entire* hypophysis, we have seen, was found by Camus and Roussy and Houssay and Hug not to be followed by polyuria. Even though this does not apply to all experimental observations, Houssay, for instance, having observed a temporary polyuria after this procedure, the fact remains that removal of the anterior lobe as well as the posterior so modifies the whole functional and metabolic activities of the body that it hardly affords dependable results. In 6 dogs subjected to this radical operation by an expert operator, Blair Bell,[79] one died under anesthesia, but the remaining 5, even though they recovered and partook of food, died in from twenty-two to thirty-six hours. They became somnolent and "although it was sometimes possible to rouse them from this condition and to get them to stand and take food, they quickly became somnolent again as soon as they were left alone. After a few hours the respirations became very slow and coma set in; finally death supervened." If it is now recalled that I^{31} have also traced a path from the hypophyseobasal area to the adrenals and that ample evidence[80] has confirmed the personal view of 1903 that the adrenals sustained tissue oxidation, the cause of death from respiratory failure by removal of the whole hypophysis becomes plain. Yet, the survivals of hypophysectomized animals recorded by Camus and Roussy, Sweet and Allen[81] and others, find a normal explanation in the fact that removal of the hypophysis leaves all the basal tissues intact as well as the bulbar vasomotor and other coördinating centers to carry on approximately (as shown by obesity or other disorders observed in operated animals) the vital processes with which the hypophyseobasal area is concerned. The vasomotor center is also a potent compensative factor in all conditions external to it that affect the circulation and produce CO_2 toxemia; it probably aided, when stimulated by the carbon dioxide, in arresting the polyuria observed in Houssay and Hug's hypophysectomized dogs, by favoring contraction of the renal arteries.

Conclusions. Swale Vincent's conclusion that the prevailing attitude concerning the functions of the hypophysis should be reconsidered in view of the labors of Camus and Roussy, Bailey and Remer, Houssay and others being fully justified, the line of research reviewed in the foregoing pages is intended to point out:

1. That it is because the functions attributed to the posterior lobe of the hypophysis by physiologists and others have been erroneous from the start that Swale Vincent's conclusion that the attitude in relation to this organ should be reconsidered now imposes itself.

2. That the investigations of Camus and Roussy and others named do not demonstrate that the posterior lobe of the hypophysis

takes no part in the pathogenesis of diabetes insipidus or polyuria; they only show that lesions of the tuber cinereum can provoke these disorders, and that the latter can be produced without the participation or need of a secretion from the hypophysis.

3. That the effects of lesions upon, the slightest contact with, or manipulation of, the posterior lobe; its embryological origin as a neural organ; its histological and chemical similarity to the cerebral cortex; the various disorders which may be strictly localized in it; its autonomous role with the overlying tuber cinereum as shown by decerebrated animals, and other facts submitted, point to this *hypophyseobasal area*, the name herein suggested for it, as the central starting point of a nerve path which then descends by way of the bulb, the cord and the splanchnic nerves to the kidneys.

4. That the experimental data recorded by Camus and Roussy and others are accounted for by the inhibition or arrest, as a result of lesions practised by them or the pathological sequels of such lesions in the tuber cinereum, of the physiological impulses through the hypophyseorenal path to the vessels of the kidneys, thus causing passive dilation of these vessels, abnormal excitation of the renal cells by the excess of arterial blood thus permitted to reach them and as end result, polyuria or diabetes insipidus.

5. That the beneficial effects of posterior pituitary preparations are accounted for, not by a supposed secretion or hormone in these products, since the actual existence of such a secretion as a physiological entity has never been demonstrated and is controverted by many facts, but by the recognized pharmacological property of these preparations of causing constriction of the arterioles, thus counteracting in the kidneys the dilation of these vessels, which dilation is the cause of diabetes insipidus and polyuria insofar as their relationship with the *hypophyseorenal nerve path*—a term I would also submit as appropriate—is concerned.

REFERENCES.

1. Vincent, Swale: Lancet, 1922, **2**, 313.
2. Camus and Roussy: Endocrinology, 1920, **4**, 507; Jour. de physiol. et de path. gén., 1922, **20**, 509, 535.
3. Bailey and Bremer: Endocrinology, 1921, **5**, 761.
4. Bailey and Bremer: Ibid.
5. Houssay and Hug: Compt. rend. Soc. de biol., Paris, 1921, **85**, 315.
6. Houssay: Endocrinology, 1918, **2**, 94.
7. Cushing: Boston Med. and Surg. Jour., 1913, **168**, 901.
8. Marañon and Rosique: Trab. de la Soc. de biol., Barcelona, 1917, **19**, 126.
9. Houssay and Roman: Prensa méd., Argentina, 1917–1918, **4**, 284.
10. Marañon: Neuvas orientaciones sobre la patogenia y tratamiento de la diabetes insipida Madrid, 1920, p. 106.
11. Dixon and Cow: Proc. Roy. Soc. Med., London, Sect. Ther. and Pharmac., 1921, **14**, 6.
12. Jacobson, C.: Johns Hopkins Hosp. Bull., 1920, **31**, 185.
13. Souques, Alajouanine and Lermoyez: Trans. Third Intern. Congr. of Neurol.; cited by Monde méd., 1922, **32**, 576.
14. Watanabe and Crawford: Jour. Pharm. and Exp. Therap., 1916, **8**, 75.

15. Rogers, F. T.: Proc. Soc. Exp. Biol. Med., New York, 1921, **19**, 125.
16. McKinlay, C. A.: Arch. Int. Med., 1921, **28**, 703.
17. Dixon, W. E.: Jour. Physiol., 1923, **57**, 129.
18. Sajous, C. E. de M.: Internal Secretions and the Principles of Medicine, 1908, 2d ed., **1**, 293.
19. Foster, Michael: Text-book of Physiology, Philadelphia, 1895, 6th ed.
20. MacArthur, A. G.: Jour. Am. Chem. Soc., 1919, **4**, 1225.
21. Luschka: Der Hirnanhang und die Schilddrüse des Menschens, 1860.
22. Müller: Jenaïsche Ztschr. f. Natur-Wissen, 1871, **6**, 354.
23. Berkley, H. J.: Brain, 1894, **17**, 515.
24. Osborne and Vincent: Brit. Med. Jour., 1900, **1**, 502.
25. Piersol: Human Anatomy, 1907, p. 1107.
26. de Cyon, E.: Pflüger's Arch., 1898, **72**, 635.
27. Masay, F.: l'Hypophyse, Thèse de Bruxelles, 1908.
28. Pirrone: Riforma med., 1903, **19**, 169, 205.
29. Sajous, C. E. de M.: Internal Secretions and the Principles of Medicine, 1903, 1st ed., **1**, 483.
30. Weed, Cushing and Jacobson: Johns Hopkins Hosp. Bull., 1913, **24**, 40.
31. Sajous, C. E. de M.: Gaz. des hôp., 1908, **81**, 339.
32. Schäfer, E. A.: Proc. Roy. Soc. Biol. (Ser. B), 1909, **80**, 442.
33. Benario, J.: München. med. Wchnschr., 1913, **60**, 1768.
34. Sequeira: Tr. Roy. Soc. Med., Dermat. Sect., Brit. Jour. Dermat., 1915, **27**, 186.
35. Berge and Schulmann: Presse méd., 1918, **26**, 618.
36. Marañon: Loc. cit., p. 58.
37. Simmonds, M.: München. med. Wchnschr., 1914, **61**, 180.
38. Neuburger: Berl. klin. Wchnschr., 1920, **57**, 10.
39. Sekiguchi: Ann. Surg., 1916, **63**, 298.
40. von Meyenburg, H.: Zieglers Beiträge, 1915–1916, **61**, 550.
41. Globus and Strauss: Arch. Neurol. and Psych., 1922, **8**, 53.
42. Newmark, L.: Arch. Int. Med., 1917, **19**, 550.
43. Luzzatto: Sperimentale, 1918, **71**, 405.
44. Chauffard: Med. Press. and Circ., 1920, **110**, 142, n.s.
45. Römer, C.: Deutsch. med. Wchnschr., 1914, **40**, 108.
46. Lhermitte, J.: Ann. de méd., 1922, **11**, 89.
47. Veil: Deutsch. med. Wchnschr., 1920, **46**, 558.
48. Leschke, E.: Ibid., 1920, **46**, 959.
49. Lecorché and Talamon: Am. Med. Digest, June, 1888; cited by Sajous: Ann. Univ. Med. Sci., 1889.
50. Ebstein, W.: Deutsch. Arch. f. klin. Med., 1909, **95**, 1.
51. Marinesco, N. W.: Arch. Orient. de méd. et de chir., 1900, **2**, 57.
52. Weiszbarth, J.: Lancet, 1888, **1**, 737.
53. Futcher: Modern Medicine, Osler and McCrae, 1914, **2**, 724.
54. Eichhorn, G.: Jahrb. f. Kinderheilk., 1896, **42**, 44.
55. Motzfeldt, Ketil: Boston Med. and Surg. Jour., 1916, **174**, 644.
56. Futcher, T. B.: Johns Hopkins Hosp. Reports., 1902, **10**, 197.
57. Lépine, R.: Diabetes Insipidus, Sajous' Analytical Cyclopedia of Practical Medicine, 9th ed., vol. 4, p, 2.
58. Ricaldini: Bull. et mém. Soc. méd. d. hôp. de Paris, 1922, **46**, 1238.
59. Beck, H. G.: Dystrophia Adiposogenitalis, Endocrinology and Metabolism, 1922, **1**, 894.
60. Hamilton: Canada Med. Assn. Jour., 1922, **12**, 209.
61. Briand and Rouquier: Bull. et mém. Soc. méd. de hôp. de Paris, 1920, **44**, 769.
62. Gosset and Gutmann: Ibid., 1921, **45**, 1674.
63. Bénard, R.: Ibid., 1922, **46**, 553.
64. Sajous, C. E. de M.: Internal Secretions and the Principles of Medicine, 1st ed., 1903, **1**, 577.
65. Salmon, A.: Sull' origine del sonno, Firenze, 1905.
66. Cammidge: Practitioner, 1920, **105**, 244.
67. Tucker, J.: Am. Jour. Med. Sci., 1922, **163**, 668.
68. Hall, G. W.: Ibid., 1923, **165**, 551.
69. Marañon: Loc. cit., p. 122.
70. Sajous, C. E. de M.: Internal Secretions and the Principles of Medicine, 1st ed., 1903, **1**, 587.
71. Brubaker: Text-book of Physiology, 7th ed., 1922, p. 632.

72. Schäfer: Text-book of Physiology, 1900, **2**, 728.
73. Mark, I. P.: Acromegaly; a Personal Experience, London, 1912, p. 28.
74. de Cyon, E.: Cited by Richet: Dictionnaire de physiologie, 1900, **4**, 131.
75. Sajous, C. E. de M.: Internal Secretions and the Principles of Medicine, 2d ed., 1907, **2**, 1001.
76. Farini, Francesco: Gazz. d. osp., Milan, 1913, **34**, 1135.
77. Weir, Larson and Rowntree: Arch. Int. Med., 1922, **29**, 306.
78. Rees and Olmstead: Endocrinology, 1922, **6**, 230.
79. Bell, Blair: The Pituitary, 1919, p. 144.
80. Sajous, C. E. de M.: Endocrinology, 1918, **2**, 258.
81. Sweet and Allen: Ann. Surg., 1913, **57**, 485.

CEREBROSPINAL FLUID IN ENCEPHALITIS LETHARGICA.

By Harold E. Foster, M.D.,
ROCHESTER, N. Y.,
AND
Jessie Reed Cockrell, A.B.,
BOSTON, MASS.

(From the Department of Pathology and Neurology, Massachusetts General Hospital.)

Although there has been more or less discussion of the sugar content of the cerebrospinal fluid since its presence in normal fluid was established on a sound basis by Nawratzki (1897) and by Denigès (1898), with the confirmatory work of Gimbert and Coulaud (1903), a more specific interest dealing with laboratory investigations as to its quantitative determination and its possible significance in relation to pathological conditions of the central nervous system has developed during the last three years. Evidence of this interest has demonstrated itself in a rather extensive literature, more abundantly from the French workers, giving the results of researches made in quantitating by various methods the sugar in both normal and abnormal cerebrospinal fluids. Since von Economo (1917, at Vienna) reported cases of encephalitis lethargica, many investigators have pursued laboratory methods of approach in studying the disease. The nature of such work was necessarily a physico-chemical study of the cerebrospinal fluid, obtained from cases giving a clinical picture simulating encephalitis lethargica. With a few exceptions, the amount of sugar in the cerebrospinal fluid of encephalitis lethargica has not received its due measure of attention. This has probably been due to the use of qualitative methods which are of slight value and which do not give sufficiently reliable results to determine either the absence or increase of sugar in the cerebrospinal fluid. Consequently, it is purposed here to present quantitative determinations which have been made on fluids from 35 cases of encephalitis lethargica. The diagnosis is

based in each case on both the clinical signs and symptoms and the laboratory results. Two cases were checked by necropsy. The 35 cases are divided into two series. The second series is a sequel to the one presented by Foster[1] from the same laboratory in 1921. The results of both series are identical in obtaining a percentage of sugar above 0.0600 per cent in all but one determination.

Among the very recently reported investigations, the consensus of results coincides with those obtained in this laboratory. Barré,[2] using the Fehling's-Durand method, regards an elevation of sugar characteristic of both acute and subacute stages of encephalitis lethargica. Bourges, Foerster and Marcandier[3] maintain that the sugar content has always been found higher than normal. Also Laporte and Rouzaud[4] state "hyperglycorachia has been constant in all the cases observed." Dopter[5] considers sugar increased in encephalitis lethargica, but not pathognomonic. Additionally, Coope[6] presents an 82 per cent increase of sugar from tests made on 95 fluids obtained from 11 cases, using the Folin-Wu method. Moreover, Eskuchen[7] parallels, with a modified Bang method, the results shown here. Thus the evidence given by these investigators supports the findings recorded in Tables I and II.

The data presented offer various points of interest; the point of striking interest tends, however, in both series to be mostly in the results of the sugar determinations. The percentage of amounts above 0.0600 per cent in Table I, is duplicated in Table II. The results were obtained by the same method, Folin-Wu,[8] in the same laboratory; one set in 1921, the other in 1922 to 1923.

The Folin-Wu method used for the quantitative determination of the amount of sugar in the cerebrospinal fluid is the same as the method for determining blood sugar, excepting a weaker standard solution is used for the cerebrospinal fluid. This is a 0.005 per cent solution of dextrose which gives a more comparable colorimetric reading than a 0.1 per cent used for blood. Foster[1] found that with some fluids the filtrate was cloudy, but it has since been found that such cloudiness may be eliminated by filtering through four filter papers. The results obtained by the Folin-Wu method give lower quantities than the results determined by the Myers and Bailey and the modified Lewis and Benedict methods, as is shown in a comparative study made by Thalhimer and Updegraff.[9] In this laboratory, the limiting amounts of sugar in cerebrospinal fluid are considered normally from 0.0400 to 0.0600 per cent.

Evidence of the source of the sugar in the cerebrospinal fluid is wanting. The existence of any relation between the sugar in the blood and that in the cerebrospinal fluid has not been established. Foster[1] did not obtain any alteration in the amount of sugar in the blood in the six determinations that were made on cases with sugar in the cerebrospinal fluid above 0.0600 per cent. Yet the opinion

TABLE I.—1921 SERIES.*

Case.	Sex.	Age.	Time since onset.	Fluid.	Cells per 1 cm. (5 per cm. for normal).	Total protein† (40 mg. per 100 cc normal).	Colloidal gold reaction.	Sugar (0.04 to 0.06 per cent normal).	Wassermann reaction.
1	M.	37	2 days	Clear. Colorless.	26	80	0011100000	0.0681	Negative.
2	M.	28	4 "		150	50	0000000000	0.0909	Negative.
			9 "		130	28	0114100000	0.1130	Negative.
3	M.	5	4 "		6	25	0122100000		
			9 "		10	26	0000000000	0.0761	Negative.
4	M.	43	1 wk.		14	42	0000000000	0.0700	Negative.
5	F.	40	1 "		18	55	0122210000	0.0810	Negative.
6	F.	29	1 "		90	47	0122100000	0.0674	Negative.
			2 wks.		90	21	0121100000	0.0620	Negative.
7	F.	26	1½ "		45	44	3355410000	0.0731	Negative.
			4 "		12	..	...	0.0695	Negative.
8	F.	10	2 "		11	25	0122310000	0.0535	Negative.
9	M.	43	2½ "		8	29	0123210000	0.0710	Negative.
10	M.	54	3 "		22	72	4455553100	0.0847	Negative.
			5 "		34	61	4443210000	0.0937	Negative.
11	M.	42	...		144	63	0000000000	0.0666	Negative.

* Foster, H. E.: Jour. Am. Med. Assn., 1921, **76**, 1300.
† Denis, W., and Ayer, J. B.: Arch. Int. Med., 1920, **26**, 436.

TABLE II.—1922–1923 SERIES.

Case.	Sex.	Age.	Time since onset.	Fluid.	Pressure in mm. H_2O (250 mm. upper normal).	Cells per 1 cm. (5 per cm. normal).	Globulin†.	Total protein‡ (40 mg. per 100 cc normal).	Colloidal gold reaction.	Sugar (0.04 to 0.06 per cent normal).	Wassermann reaction.
1	F.	24	3 days	Clear. Colorless.	185	0	+	33	0000000000	0.0576	Negative.
2*	M.	74	Few "		216	115	−	47	0001221000	0.0727	Negative.
3	M.	33	1 wk.		168	15	Sl. +	48	0000000000	0.0917	Negative.
4	F.	16	1½ wks.		140	4	−	29	0000000000	0.0928	Negative.
5	M.	30	2 "		150	39	Sl. +	67	0000000000	0.0689	Negative.
			2½ "		100	12	−	58	0000000000	0.0800	Negative.
6	M.	20	2½ "		60	0	−	36	0000000000	0.0701	Negative.
			3 "		120	2	Sl. +	52	0000000000	0.0700	Negative.
7	M.	27	2½ "		100	1	Sl. +	60	1333320000	0.0730	Negative.
8	F.	20	3 "		180	4	+	50	0000000000	0.0720	Negative.
9	M.	43	3 "		...	4	+	47	000000000.	0.0730	Negative.
10	F.	35	3 "		150	7	−	37	0000000000	0.0980	Negative.
11	M.	51	3 "		130	2	−	33	0000000000	0.0740	Negative.
12*	M.	30	3 "		...	4	+	67	...	0.1030	Negative.
13	F.	38	3 "		175	1	−	35	0000000000	0.0719	Negative.
14	M.	36	3½ "		145	34	−	41	0000000000	0.0724	Negative.
15	F.	28	4 "		50	34	+	54	0000000000	0.0707	Negative.
16	M.	26	4 "		...	32	+	51	0000000000	0.0724	Negative.
17	F.	28	5 "		115	7	+	48	0000000000	0.0645	Negative.
18	M.	36	2 mos.		140	2	−	33	0000000000	0.0645	Negative.
19	F.	26	2½ "		50	44	−	40	0000000000	0.0740	Negative.
20	M.	20	3 "		180	5	Sl. +	67	0000000000	0.0500	Negative.
21	M.	19	21 "		250	3	Sl. +	55	1123321000	0.0606	Negative.
22	M.	63	2 yrs.		100	3	+	67	0000000000	0.0714	Negative.
23	M.	23	3 "		120	2	−	45	0000000000	0.0625	Negative.
24	F.	33	4 "		35	2	−	50	1112321000	0.0657	Negative.

* Nos. 2 and 12 confirmed by necropsy.
† Ross-Jones test with saturated sol. ammonium sulphate.
‡ Denis, W., and Ayer, J. B.: Arch. Int. Med., 1920, **26**, 436.

THE RESULTS OF THESE 2 TABLES MAY BE SUMMARIZED BRIEFLY:

No. of cases.	Pressure over 250 mm. H_2O, per cent.	Cell count over 5 per cm., per cent.	Presence of globulin, per cent.	Total protein over 40 mg. per 100 cc, per cent.	Colloidal gold reaction, per cent.	Sugar over 0.06 per cent.
Table I (11)	...	100.0	...	72.8	72.8	91.0
Table II (24)	0.0	41.6	58.3	75.0	16.0	91.0

of the French investigators tends toward a belief that there is a definite relationship existing between the presence of sugar in the blood and in the cerebrospinal fluid. This viewpoint is held by Laporte and Rouzaud,[4] who obtained a hyperglycemia simultaneously with a hyperglycorachia in cases of encephalitis lethargica. Likewise, Bourges, Foerster, Marcandier[3] report "glycemia parallels glycorachia." Dopter[5] considers the increase of the amount of sugar in the cerebrospinal fluid to be influenced by an increased amount in the blood. Moreover, Polonovski and Duhot[10] report simultaneous changes found experimentally between the sugar levels in the blood and the spinal fluid. In contradiction to the above observations, Eskuchen[7] fails to note any relation between the sugar of the cerebrospinal fluid and that of the blood. It is obvious that further research work on the source and function of the sugar in the cerebrospinal fluid is necessary.

Another question is whether the amount of sugar obtained in encephalitis lethargica is a true increase or is only a high normal. The following observation favors the possibility of its being an increased amount: In 225 sugar determinations made in this laboratory during the past twelve months the amounts above 0.0600 per cent were all in fluids, which gave other abnormal reactions. The fluids were from cases of a variety of pathological states, as gas poisoning, feeble-mindedness, brain tumor, metastatic tumor of the spinal cord, septicemia and tabes dorsalis. Therefore, the amount of sugar in the cerebrospinal fluid of encephalitis lethargica is not preferred as pathognomonic of the disease. None the less, it is presented as having diagnostic value in the study of laboratory findings.

In encephalitis lethargica, the fact that the sugar content of the cerebrospinal fluid is the most constantly positive laboratory result, the fact that it is the most striking finding in viewing the cerebrospinal fluid as a whole, indicates the possibility of its being useful in the hands of clinicians. In a cerebrospinal fluid, as Case IV in Table II, showing a clear, colorless fluid under a pressure of 140 mm. of water, 4 cells per cm., no globulin, 29 mg. of total protein per 100 cc, no change in the colloidal gold test, and a negative

result in the Wassermann reaction, but *showing* 0.0928 *per cent of sugar* and with clinical symptoms suggesting encephalitis lethargica, the quantity of sugar is obviously important. This illustrative example is amplified by an analysis of the findings recorded in Tables I and II.

In Table I, the observations were made on fluids from 11 cases, the duration of the disease since onset being from two days to five weeks; although all cell counts are above 5 cells per cm., none the less no one estimation is above 150; and the largest amount of total protein is 80 mg. per 100 cc; the colloidal gold reaction is given in more cases than in Table II. Whereas the percentage of sugar content is exactly the same as that obtained in the results shown in the second table.

A study of Table II shows a record of 24 patients, with the duration since the onset of clinical symptoms extending from three days to four years, on whom clear, colorless cerebrospinal fluid was obtained under normal pressure. The cell-count is in over 50 per cent of the number of fluids below 5 per cm. with the highest count 115. The presence of some globulin in 58 per cent with the quantitative amount of total protein showing an increase over 40 mg. per 100 cc in 75 per cent. The normal range of total protein is considered to be from 15 to 40 mg. in 100 cc of cerebrospinal fluid by the Denis-Ayer method.* The colloidal gold gives a low percentage of reaction, and in cases giving a curve it is one in the "luetic" zone. The fact of interest in the whole picture is the quantity of sugar. This is above 0.0600 per cent in 91 per cent of the fluids studied.

Emphasis should also be placed upon the part sugar in encephalitis plays in separating this condition from tuberculous meningitis. The clinical picture of the two may cause confusion in diagnosis. Observation of the results in the laboratory from a thorough study of the cerebrospinal fluid reveals characteristic differences between the two. These differences show in comparing Table II with Table III:

TABLE III.—TUBERCULOUS MENINGITIS.

Case.	Cells, 1 cm.	Total protein, mg. per 100 cc.	Colloidal gold reaction.	Sugar, per cent.
1	230	118	0001331000	0.0321
2	325	500	0003444210	0.0400
3	200	100	0000455442	0.0100
4	210	77	1123455210	0.0250
5	150	160	0002222200	0.0410
6	485	400	0000000000	0.0364
7	62	138	0000000000	0.0006
8	203	235	0012333110	0.0010
	202	236	0000122100	0.0010
9	106	500	0001122222	0.0010
10	119	190	0000000000	0.0010
11	210	400	0012333210	0.0350

* Denis, W., and Ayer, J. B.: Arch. Int. Med., 1920, **26**, 436.

Table III shows the findings in fluids from 11 cases of tuberculous meningitis: The cell count is high, globulin is present, the total protein is increased, the colloidal gold test is inconstant. Again, it is the quantity of sugar that is interesting, for it is the point of greatest divergence between the laboratory results of the two conditions. The amount of sugar in tuberculous meningitis is always low. In Table III, 45 per cent of the estimations are below 0.0010 per cent. This reduction of sugar in the fluid of tuberculous meningitis is confirmed by reports in the literature.[11]

Likewise, in cases of acute purulent meningitis all accounts reported by laboratory workers agree that there is an even more marked diminution of sugar than in tuberculous meningitis. The number of fluids examined in this laboratory are few, but the results are tabulated for the sake of completeness. (Table IV.)

TABLE IV.—ACUTE PURULENT MENINGITIS.

Case.	Cells, 1 cm.	Total protein, mg. per 100 cc.	Colloidal gold reaction.	Sugar, per cent.
1	6,800	160	0003555400	0.0000
2	2,500	366	0000000000	0.0000
3	3,000	800	0000122321	0.0000
4	13,416	1320	0000000000	0.0000
5	8,000	500	0000111110	0.0000

Finally, it may be suggested that in other conditions, giving no specific test, as the Wassermann reaction in syphilitic meningitis, but showing symptoms that cause confusion with encephalitis lethargica, a quantitative study of the sugar in the cerebrospinal fluid offers a possibility of differential significance. There have been other conditions diagnosed here encephalitis lethargica. From one case a clear, colorless spinal fluid showed 3 cells per cm. 55 mg. of total protein per 100 cc, a colloidal gold curve of 1123210000; both spinal fluid and blood gave negative Wassermann results. The patient developed Jacksonian epileptic convulsions. Another case gave a clear, colorless spinal fluid that had 11 cells per cm. 56 mg. of total protein per 100 cc, a slightly positive globulin test, a negative colloidal gold curve, and a negative Wassermann reaction. This patient had alcoholic poisoning. Both of these cases presented clinical pictures compatible with encephalitis lethargica. These are noted here only in that it seems likely that such confusion might have been lessened by adding to an otherwise careful study of laboratory findings of the cerebrospinal fluid a quantitative estimation of the sugar content. Confusion in diagnosis caused by an "encephalitic syndrome" is noted in the literature. Hassin[12] reports veronal poisoning; Bassoe[13] a case of brain tumor; and Hamill[14] calls attention to a case of syphilitic involvement of the central nervous system with a negative Wassermann reaction.

A high sugar is not, as has been said previously, pathognomonic of encephalitis lethargica; a normal sugar is, however, obtained rarely; and a low sugar is, within the experience of this laboratory, unknown.

Conclusions. The main points to be considered from a study of the quantitative sugar determinations made on the fluids from 35 cases of encephalitis lethargica are:

1. The determination of the sugar content of the cerebrospinal fluid should be made by a reliable quantitative method.

2. An amount of sugar above 0.0600 per cent was obtained in 91 per cent of the fluids studied, using the Folin-Wu method.

3. Quantitative sugar estimations are valuable in differentiating encephalitis lethargica from tuberculous meningitis and as an aid in other conditions presenting similar symptoms.

4. The amount of sugar present in the cerebrospinal fluid is not pathognomonic of encephalitis lethargica but is of recognized utility in making the diagnosis.

BIBLIOGRAPHY.

1. Foster, H. E.: Jour. Am. Med. Assn., 1921, **76**, 1300.
2. Barré, J. A.: Bull. méd., Paris, 1921, **35**, 366.
3. Bourges, H., Foerster and Marcandier, A.: Compt. rend. Soc. de biol., 1920, **83**, 914.
4. Laport and Rouzaud: Compt. rend. Soc. de biol., 1920, **83**, 392.
5. Dopter, C.: Bull. de l'Acad. de méd., 1920, **83**, 203.
6. Coope, R.: Quart. Jour. Med., Oxford, 1921, **15**, 1.
7. Eskuchen, K.: Ztschr. f. d. ges. Neurol. u. Psychiat., 1922, **76**.
8. Folin, O.: Laboratory Manual, 1922.
9. Thalhimer, W., and Updegraff, H.: Jour. Am. Med. Assn., 1922, **78**, 1383.
10. Polonovski and Duhot: Presse méd., Paris, January, 1923, **31**, 60.
11. (*a*) Mestrezat, W.: Compt. rend. Soc. de biol., June, 1919, p. 1089.
    (*b*) Martin, W. B.: Virginia Med. Month., 1922, **48**, 689.
    (*c*) Schloss and Shroeder: Am. Jour. Dis. Child., 1916, **9**, 1.
    (*d*) Jouin, A.: Bull. de l'Acad. de méd., Paris, 1921, **80**, 594.
    (*e*) Parrot, H. W.: Lancet, London, 1919, **2**, 998.
    (*f*) Moriez, A., and Pradal, P.: Bull. et mém. Soc. méd. de hôp. de Paris, 1920, **44**, 738.
    (*g*) Prince, A.: Encephale, Paris, 1920, **1**, 384.
    (*h*) Page, M.: Gaz. d. hôp., 1920, **90**, 171.
12. Hassin, G. B.: Jour. Am. Med. Assn., 1920, **75**, 671.
13. Bassoe, P.: Arch. Neurol. and Psychiat., 1920, **55**, 118.
14. Hamill, R. C.: Med. Clin. North America, 1919, **3**, 67.

A POSSIBLE RELATIONSHIP BETWEEN THE CURRENT OF INJURY AND THE WHITE-BLOOD CELL IN INFLAMMATION.*

By Harold A. Abramson, M.D.,

NEW YORK.

(From the Laboratories of the Department of Surgery, College of Physicians and Surgeons, Columbia University, New York.)

The study of inflammation has resulted in the formulation of many hypotheses of the causes and the results of the processes present. For the purposes of the experiments upon which this

* Received for publication, July 18, 1923.

paper is based, inflammation is regarded as a process incidental to some injuries in living tissues; more particularly, the congregating of cells in the zone of injury is considered the essential feature. There is inflammation, and there must be present in the tissue where the process occurs some system of factors which brings certain tissue units to the point of injury, and the cells influenced must be able "mechanically" to reach the point of excitation. The questions of how and why the white-blood cell arrives at the point of injury have been widely discussed. Neglecting the teleological attitude, and without going into a discussion of chemotaxis, surface tension, and so on[1, 2] which have been offered as possible explanations and which certainly may play a part, this paper, first, will endeavor to offer an hypothesis which will eventually attempt to correlate qualitatively and quantitatively the chemical and mechanical make-up of tissues with the migration of the white-blood cell to some points of injury; secondly, will present some experimental evidence in favor of this hypothesis; and thirdly, in discussion will elaborate upon the first two.

I. The Basis of the Hypothesis. Although all injuries to cells or tissues are not followed by the microscopical picture of inflammation, inflammation is always an expression of injury. When living tissues are injured, whether the fashion be crushing, burning, cutting, or chemical, there ensue the visual and chemical changes which follow such interruptions of normal tissue metabolism. If a living leaf be cut, and non-polarizable electrodes be applied to both injured and uninjured surfaces,[3] there is experienced an electro-motive force between the cut and uncut surfaces. Similarly, if a carefully dissected frog's muscle be cross-sectioned, and non-polarizable electrodes be applied in the same fashion, the injured surface becomes electro-negative and the galvanometer's deflection slowly increases to a maximum, after which it suffers a parallel diminution until it eventually disappears. This current of injury varies with the point of application of the electrode upon the uninjured surface, and is not one due to membrane potential phenomena alone, but because of the fact that between the injured and normal tissue there passes when injury is produced, a more or less constant current which varies in intensity as the many factors of tissue and tissue injury do. Uninjured muscles in the resting state are iso-electric; no difference of potential is manifested at their surfaces.[4, 5]

Hermann, who made the observations noted above, formulated the law which is applicable to all cases, that, "In every injured muscle fiber the surface of demarcation between the living and dead (or rather dying) portion of the fiber is the seat of an electro-motive force toward the living part." Another related fact brought out by this author is that a general rise of temperature increases the strength of this demarcation current up to a certain limit beyond which it decreases again, until it disappears with the onset of heat rigor.

In the same fashion the currents that can be led off to a galvanometer from an artificial cross-section and from any given point of the uninjured longitudinal surface of a nerve increases, and then decreases one-half in two to four hours. But the difference of potential may increase again, and the current regain its original force if a new section is made near the first.[6] This fact is important because it seems that the strength of the current is not only influenced by temperature at the site of injury, but also the degree of the lesion. The strength of these demarcation electro-motive forces varied from .02 to .03 of a volt in the frog's sciatic nerve, and was equal to .008 of a volt in that of a horse (Biederman) . It has been known to exceed .08 of a volt in a frog's gastrocnemius (Du Bois Raymond)[7]

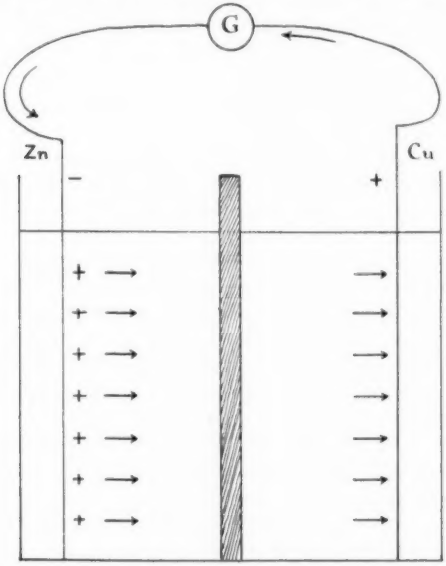


FIG. 1.—Schema to show direction of current in battery.

The significance of these currents of injury in relation to the theory of leukocyte mobility and to inflammation soon to be discussed, is more readily appreciated if the injured tissue and the adjacent normal or nearly normal cells be compared to an electric battery.[8] From the facts enumerated above it is apparent that injury to living tissues precipitates primarily an increase in chemical activity, one of the manifestations of which is the electrical phenomena observed. This increase in chemical activity may be compared to that which takes place in a battery having zinc and copper plates as electrodes which are immersed in solutions of their respective salts and separated by a porous partition.

1. The pole[9] on the left becomes negatively charged on account of the departure of positively charged ions from its surface, for this metal, zinc, goes into solution more rapidly than does copper. A current therefore, according to conventional usage, flows from positive to negative through the wire and in the form of migrating ions from positive to negative through the liquid.

2. The difference in potential (E. M. F.) is not affected by changes in the size or shape of the poles or the amounts of the solution, provided the materials are not changed. It is very noticeably altered, however, by changes in the concentrations or the type of solution.

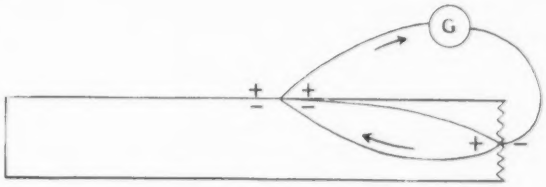


FIG. 2.—Schema to show path of demarcation current.

To resume the comparison of an injured tissue to a battery, the uninjured surface may be considered the positive pole and the injured the negative, the current flowing externally from positive to negative. Internally, the injured tissue may be compared to the immersed zinc plate—the normal to the immersed copper plate and hence the injured area will be electro-positive—the uninjured electro-negative, and the current flow from the injured to the uninjured cells.

If there be between the normal and injured tissues a current flowing which would vary with the type of tissue, degree of injury, temperature of the part, and if in this electrical field there be free cells and injured bloodvessels, the hypothesis, that one of the forces guiding the white-blood cell to the point of injury (and perhaps even playing a dominant role) is the electrical current flowing between the injured and uninjured tissues, is hardly without reason. The concept that the white-blood cell may go toward one pole or another is not new. But the pole to which they migrate has not been settled. For the past thirty years numerous observers have disagreed because the experimental conditions under which they worked were different. Platinum poles instead of non-polarizable electrodes were used; sugar or other solutions held the blood cells in suspension.[10 11 12] The hydrogen-ion concentration of the medium was neglected. The knowledge of the influence of PH on cataphoresis and proteins in general is a recent acquisition.

The technic to be described obviates as far as possible the errors mentioned above, and although the experiments to be presented

were done *in vitro*, it is fair to draw some parallelism between them and the changes in the living tissue. Unglazed porcelain non-polarizable boot electrodes were set in a glass block 5 mm. apart and ground down so that the level of the electrodes and glass were the same. The apparatus was kept in physiologically normal saline whose pH was about 7.5, approaching that of serum. While on a warm stage at about 100° F., the effect of the passage of a current from a dry cell through human serum containing the cells of the uppermost layer of centrifuged defibrinated blood was observed. The coverslip over the drops was surrounded by paraffin, and thus preventing evaporation, preparations could be studied for hours. A shunted galvanometer recorded the passage of the current and a pole changer was in the circuit.

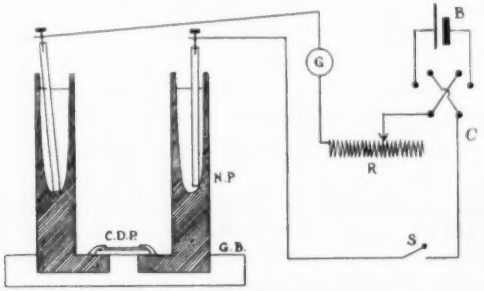


FIG. 3.—Diagram of apparatus; *B*, battery; *C*, commutator; *C.D.P.*, coverslip and serum surrounded by paraffin; *G*, galvanometer; *G.B.*, glass block; *N.P.*, non-polarizable electrodes; *R*, rheostat; *S*, switch.

II. Experimental Evidence. The following observations have been made with the technic which was described most briefly in the preceding paragraph.

1. Small lymphocytes, when the estimated difference of potential between the two electrodes is .4 of a volt and the current through the circuit $\frac{1}{25}$ of a milliampère, migrate toward the positive pole with a speed approximately of 15 microns per minute.*

* There are numerous technical difficulties attached to the use of the apparatus described in these experiments. A recent article by Winslow *et al* (Jour. Gen. Physiol., 1923, **6**, 177) takes up some of these, and gives rather complete references to the theoretical considerations. The presence of glass particularly influences the speed of migration of particles suspended in a watery medium. Water is electro-positive to glass. "That is, the water which moves toward the cathode at the glass surfaces returns toward the anode in the mid-regions of the fluid in the cell. Obviously then, the electrophoretic movement of the particles will be impeded at certain levels in the cell and accelerated at others by the independent movement of the water. In addition, of course, there is the electrical endosmose, due to difference of potential between the particles and the water. The true mobility of the particles is the average mobility of all levels in the cell."

In the experiments of the author there were many mechanical drawbacks, especially the tendency of the white-blood cells to settle upon the glass block, thus preventing an attempt to determine "the true mobility of the particles"—the lympho-

They move faster than red blood cells in the same preparation, pushing them aside and traveling almost in a straight line. When the current is reversed they almost instantaneously change the direction in which they are traveling. All the lymphocytes in the field do not migrate. Those which seem physically able to do so invariably travel toward the positive pole, or, comparing it to the injured tissue, to the electrical equivalent of the point of injury. Although tiny processes seem to be thrown out, there could hardly be said to be much, if any ameboid motion, and the migration could in all probability be considered a result of cataphoretic phenomena.

The speed of migration was not dependent upon the "age" of the lymphocyte. Approximately the same velocity was shown by lymphocytes which were obtained from freshly drawn blood and by those which had been kept on ice for thirty hours or less.

2. Polymorphonuclear leukocytes, under the same conditions, exhibited nothing which could be called a constant direction of migration. The experiments were entirely negative as far as this type of blood cell was concerned. Since unicellular organisms, including ameboid forms, in general under the proper electrical and mechanical conditions move toward one pole or the other,[13, 14, 15, 16, 17, 18] it should be expected that the movements of the polymorphonuclear leukocyte would also be influenced by the galvanic current. At present a direct analogy cannot be made with the ameba because the observations were not made under known conditions of hydrogen-ion concentration. The effects of glass and of the presence of light, the absence of chemical substances accompanying tissue injury, the need of a stronger current and the mechanical conditions may influence ameboid movement in the leukocyte. In this connection, the effect of glass on the cataphoresis of bacteria,[19]

cytes. The cells whose average speed was 15 microns per minute were those which moved. There were also present in the field red blood cells and leukocytes, although an attempt was made to get only white blood cells from the uppermost layer of the defibrinated human blood with delicate capillary pipettes. Many of the lymphocytes, particularly those resting on the glass, exhibited no movement in either direction. Those which did move always moved toward the anode. Hence the figures given in this report for lymphocytic speed under the experimental conditions is not the "true mobility" of the lymphocyte under those conditions, but is an expression of the direction of migration of the lymphocyte, aided in speed, presumably, by the anodal flow of water in the mid-regions of the cell.

In the Helmholtz-Lamb equation,

$$\text{P.D.} = \frac{4\,n\,v\,n}{K\,X}$$

in which:

n = viscosity of the solution.
v = velocity of the particle in centimeters per second.
K = dielectric constant of the solution.
X = potential gradient.

All electrical units expressed electrostatically, *cannot* be used with the figures reported for the speed of the lymphocytes to determine the potential difference (P.D.) between the lymphocytes and the serum in which they were suspended, because of a lack of knowledge of their "true mobility."

the influence of light on the ameba,[20] the change in direction of migration of paramecium brought about by chemical substances[21] are both interesting and important. For in all probability these factors and the mechanical limitations (*e. g.*, polymorphonuclear leukocytes upon meeting a roughened crack in glass almost invariably ceased to move) play an important role in the failure of the experiments. Even tissue cultures grow in line with a constant current and perpendicular to a conductor.[22] The applicability of this work to the repair of tissue injury, to the growth of bloodvessels into granulation tissue and its own formation, is most suggestive when considering the electrical phenomena incidental to injury.

III. The Elaboration of the Theory. Several questions have been asked. Will leukocytes under the experimental conditions react to a stronger current? Are the mechanical conditions present conducive to migration? Does light inhibit their response to the electric current? That is, under the experimental conditions may there not have been many other factors which influence the direction of the leukocytic migration over the pathway described and that observed be a resultant of these forces?

In answer, the following elaboration of the theory is presented purely as speculation based upon the physiology and pathology of inflammation as well as what has been described. In the presence of an acute infection* there are manifested the signs of an increase in chemical activity, and were the demarcation current to be measured, it should be greater than that produced by a low grade inflammatory process. In terms of the current of injury therefore, chemical phenomena are set up in the chronic process which do not produce as intense a current as in the acute process. With a weak constant current are attracted the slow moving lymphocytes; with the stronger current, the greater tissue injury, and perhaps with the production of leukocyte stimulating substances there rush, directed by the demarcation current plus the other factors, the leukocytes and some lymphocytes. As the chemical activity abates and the leukocytes disintegrate, there remains a small but constant current sufficient to maintain a steady lymphocytic migration. And with the further waning of the electrical phenomena, there are fewer and fewer white-blood cells wandering to the site, until with the cessation of the current, the migration ends.

In further support of this point of view is the reaction of the tissues themselves. If they be listed according to the ease with which an inflammatory process be set up within them, it will be found to be a function of the chemical response to injury and hence a function of the demarcation current. That is, connective tissue responds more readily than cartilage to injury, tendon less than connective tissue. The character of chemical make-up of the tissue

* Or any severe injury.

produces a great number of physical and chemical changes in response to injury, the resultant of which is an index of what the demarcation current would be. Experiments by W. C. Clarke and W. C. Woolsey lead one to suspect that hyaline cartilage does not respond to injury by the usual process of repair. A summary of one of the experiments follows: In dog No. 116/85, January 28, 1914, forty-nine days after incision of the cartilage of the humeral head, the surface appeared grossly as if no attempt at repair had taken place. Microscopical examination bore out the gross findings. A "V"-shaped defect into the cartilage, but not through to the underlying bone, revealed no morphological suggestions of repair or change in the surrounding cartilage cells.

If the injury had been one that involved a greater chemical response would the microscopical reaction have been different?

The mechanical limitations to reaction within a tissue like tendon or cartilage also plays its part. Even if the current were strong enough in cartilage, which apparently does not set up a true "chondritis," could the white-blood cell overcome the resistance offered by the poor transits for cellular migration?

The following further experiments would partially determine the appropriateness of the outlined hypothesis.

1. The study of the response of leukocytes and lymphocytes to different currents and electro-motive forces under varying conditions (*e. g.* in the presence of extract of tissue, etc.).

2. The measurement of the demarcation currents of different tissues under standard conditions and their comparison with those used experimentally.

3. The demonstration of the effect of the electric current *in vivo*.

4. The reaction of clinical material treated by the principles of the inflammatory process as cited above.

Summary. 1. A theory is offered that one of the forces guiding the white blood cell to a point of injury followed by an inflammatory process may be the current of injury (demarcation current).

2. With non-polarizable electrodes under stated conditions, small lymphocytes migrate toward the anode which may apparently be compared to an injured tissue focus where inflammation has set up.

3. Polymorphonuclear leukocytes under the same conditions do not consistently go toward one pole or the other. The probable cause of their failure is discussed.

4. The speed of 15 microns per minute manifested by small lymphocytes was the same whether freshly drawn blood cells were studied, or those taken from defibrinated blood kept on ice up to thirty hours.

5. Little if any ameboid motion was observed during lymphocytic migration.

6. Those tissues which respond most easily with the picture of inflammation to injury, should have the greatest currents of injury, thus correlating the view expressed with the pathological processes.

7. The mechanical and chemical make-up of tissues is stressed as a deciding factor in ease of production of the picture of inflammation.*

BIBLIOGRAPHY.

1. Zinsser, H.: Infection and Resistance, MacMillian Co., New York, 1919, p. 85.
2. Wells, H. G.: Chemical Pathology, W. B. Saunders Company, Philadelphia and London, 1920, p. 247.
3. Biederman, W.: Ergebnisse d. Physiol., 1903, **2**, 264.
4. Hermann, D. L.: Handbuch der Physiol., 1879, **1**, 192.
5. Biederman W.: Elecktrophysiologie, Jena, 1895, p. 274.
6. Du Bois Raymond: Untersuchungen über thier. Elect., Berlin, 1848.
7. Du Bois Raymond: Quoted by Luciani L. (Trans. by F. A. Welby) MacMillian & Co., London, 1915, **3**, 75.
8. Waller, A. D.: Lectures on Physiology, Longmans, Green & Co., London, 1897, p. 1.
9. Smith, A.: Inorganic Chemistry, Century Co., New York, 1915, p. 667.
10. Putter, E.: Ztschr. Immunitat., 1921, **32**, 538.
11. Dineur: Bull. Soc. belge de micro., 1891-92, **28**, 113, quoted by Putter, E., Loc. cit., p. 539.
12. Lillie, R. S.: Am. Jour. Physiol., 1903, **8**, 273.
13. Verworn, M.: General Physiology, MacMillian & Co., London, 1899, pp. 455–460.
14. Pearl, R.: Studies on Electrotaxis I, Am. Jour. Physiol., 1900, **4**, 96.
15. Jennings, H. S.: Contributions to the Study of the Behavior of Lower Organisms, Carnegie Institute, Washington, 1904, p. 191.
16. Loeb, J.: Forced Movements, Tropisms, and Animal Conduct, J. B. Lippincott & Co., Philadelphia and London, 1918, p. 41.
17. Kosaka and Siki: Quoted by Putter, E., Loc. cit., p. 539.
18. Putter, E.: Loc. cit.
19. Putter, E.: Loc. cit.
20. Schaeffer, A. A.: Reaction of Amœba to Light, Science, 1914, **39**, 474.
21. Bancroft, L. W.: The Control of Galvanotaxis in Paramœcia by Chemical Substances, University of California Publications in Physiology, 1906, **3**, 21.
22. Ingvar, S.: Reactions of Cells to the Galvanic Current in Tissue Cultures, Proc. Soc. Exp. Biol. and Med., 1919–20, **17**, 198.

PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF PATIENTS PRESENTING ESSENTIAL HYPERTENSION.†

By Ernest S. du Bray, M.D.,
INSTRUCTOR IN MEDICINE, UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL.

Origin of the Conception of Essential Hypertension. The evolution of instruments for the precise and ready measurement of blood-pressure during the past two decades, combined with the simultaneous introduction of numerous laboratory procedures devised

* The author desires to express his sincere thanks to William C. Clarke, and Arthur P. Stout, of the Department of Surgery and to Professor Horatio B. Williams, of the Department of Physiology, for the aid and criticisms received during the experimental work and the writing of this paper.

† Read before the Medical Society of the State of California, General Medical Section, June 22, 1923.

for the estimation of kidney function, have served to direct attention to a rather large and important group of cases, free from organic changes beyond cardiac hypertrophy and altered vessels, which we have come to designate, essential hypertension.

By this term is meant a state of primary vascular hypertension without the co-existence of demonstrable renal impairment as can be determined by any test of kidney function. Numerous other terms have been applied to this condition, with the idea of defining it more accurately, among the better known of which are, the hyperpiesa of Allbutt,[1] benign hypertension of Vaquez, and the hypertensive cardio-vascular disease of Janeway.

Because of its great frequency, obscure origin and pathogenesis, and its suspected relation to vascular, cardiac and renal disease, interest in this condition has been untiring.

In recent years a modified view of the significance of hypertension has arisen, so that it is no longer regarded as a disease, but rather as a symptom, however, not a constant symptom of any one malady. Hypertension is, therefore, analogous to fever.

What are the Underlying Factors in the Production of Hypertension? Since Richard Bright, in 1836, described the disease which has since borne his name, most physiologists have agreed on one fundamental conception in the mechanism of vascular hypertension. The conception to which I refer, is an increased peripheral resistance in the vascular bed. Today, the chief controversy relates to the manner in which this is produced. Broadly speaking, two essential ideas have dominated the views of clinical pathologists since the time of Bright, the first explained the increased peripheral resistance primarily on a chemical basis; the second, advocated a mechanical origin. In current medical discussions, we find Foster of New York tending to adhere to the supposition of an unknown toxic substance in the circulating blood. This hypothetical substance is assumed to result, either from an infection, or it is the product of a disturbed metabolism. It has a pressor action, causing a vaso-constriction of the arterioles. On the other hand, Moschcowitz supports the mechanical conception and contends that structural, sclerotic, arteriolar lesions cause a narrowing of the vascular bed. This anatomical-pathological alteration secondarily gives rise to a compensatory, circulatory reaction, which is manifested by a rise in blood-pressure.

If we carry our analogy between hypertension and fever further, a broader conception of the primary process is suggested. We know that fever can be produced by several causes, chiefly however, by infection. Is it not possible, therefore, that hypertension may have various underlying causes? Christian's careful and prolonged clinical observations have lead him to the belief, that vascular hypertension is a disturbance of the cardio-vascular mechanism, arising from a multiplicity of causes.

A rational therapy of any disease begins with a complete under-

standing of the fundamental cause. Unfortunately, we have not attained this goal in essential hypertension, and for this reason it behooves us to keep our views in the fluid state until the real nature of this condition has been shown. The management of essential hypertension must, therefore, be largely on an empiric basis. Not withstanding this, there is a growing feeling among medical men interested in this subject, that much can be accomplished in the early cases by preventing premature and unnecessary breakdowns.

What are the Reasons that the Early Management of EssentialHypertension is of Especial Importance? Thanks to the pioneer studies of such clinicians as Sir Clifford Allbutt[1] and the late Theodore Janeway,[2, 3, 4] we are informed of the progress and the end stages of the hypertensive process. Janeway's extensive and accurate observations are particularly illuminating, and show that death among patients in private practice, occurs in the following ways, arranged in the order of their frequency: (1) By gradual cardiac insufficiency; (2) with uremic symptoms; (3) apoplexy; (4) from some complicating acute infection; (5) in an attack of angina pectoris. For this reason essential hypertension offers an unusual opportunity for the study and control of early disease. A large number of the patients are seen in the incipient stage of the process and if properly managed before too great strain has been imposed on the circulatory apparatus, much can be done to arrest, modify and retard the process.

Proposed classifications of this condition are numerous, but their adoption is hazardous, and particularly dangerous from the standpoint of management, because of the false sense of security they foster.

For clarity and convenience, I will divide my discussion into two parts; the first will deal with the management of the early stage, the second will deal very briefly with the advanced and late stages.

The Early Stage of Essential Hypertension. In the early stage our first duty lies along comprehensive lines, in that it aims to educate the patient in a hygienic manner of living. Fortuitously discovered in the course of routine medical examinations, the majority of the early patients are asymptomatic, and consequently do not consider themselves sick. This fact may lead to half-hearted coöperation, unless the significance and the nature of the process as we know it, is not discussed clearly and frankly, at the time it is discovered. The utilization from the outset of broad psychotherapy is essential, confidence and hope must be inspired and undue fears dispelled. The realization that the height of the blood-pressure, is of far less importance than the conditions which underlie it, must be firmly established.

The Importance of an Intimate Knowledge of the Patient's Daily Life. The important guides in the management of essential hypertension are derived from an intimate knowledge of the patient's

daily life. This is best acquired by a careful history directed to ascertain the type and the surroundings of his work, the amount, kind, and regularity of food, the personal habits, the amount and kind of exercise, the presence of nervous strain and excitement, the amount of recreation, the hours and regularity of sleep, the frequency and length of vacations, and other such details. The importance of these facts as a basis for planning a regime which will be at once practical, acceptable and beneficial to the patient cannot be over-estimated.

Rest and Relaxation. In the early cases complete rest in bed for prolonged intervals is never necessary; however, a short preliminary period of complete rest may be advantageous for patients showing evidence of circulatory strain. A change of occupation may be advisable, but usually this can be avoided by a reduction of the number of working hours per day, or the introduction of rest periods after meals. Complete relinquishment of business is rarely advisable, since loss of interests and physical inactivity often hasten deterioration and may lead to disaster. The assumption of new enterprises with increased responsibilities, should be discouraged. The great value of regular vacations at frequent intervals is often overlooked, but it is one of our most valuable assets in the management of these patients. Regular hours for sleep must be established, and not infringed upon. Errors of refraction, with a resulting eyestrain, are a frequent source of irritation and should be corrected. The morning saline or small doses of mineral oil are often helpful in regulating the bowels. Hurry and worry must be reduced to a minimum, and a mental state of composure and serenity cultivated.

Exercise and Recreation. Systematic exercise is necessary, and particularly important for the maintenance of circulatory efficiency. Out-of-door activities, such as golf, hiking, swimming, horseback riding and gardening are all excellent forms of exercise for the early patients. Besides being less irksome than any form of calisthenics, they have the added psychic value of promoting mental relaxation and diversion. Needless to say, moderation in any form of exercise should be practised and unpleasant symptoms, arising in the course of physical exertion, should remind the patient of his limitations. Strenuous physical training for competitive sports or spasmodic week-end orgies of physical activity are detrimental. In planning the program of exercise, I find Walter Camp's[8] recent book useful. It contains, among other helpful suggestions, the famous daily dozen exercises, which are readily learned and offer a good substitute to out-of-door diversions, when these are not practical. The acquisition of interests outside of the daily routine is to be encouraged, and for this reason the cultivation of hobbies and tempered enthusiasms play a real part in keeping one fit, and leave less opportunity for useless introspection.

The Problem of Dietary Regulation. Until recently the question of the dietary regulation has formed the main theme in the discussion of the management of these patients. This has resulted from our inability to divorce the nephritic problem of therapy from that of essential hypertension. In my experience no rigid restrictions in the diet are necessary in the early cases, except in those who habitually abuse food. Monotonous and limited diets work a real hardship on patients with this condition, and they are not necessary. Certainly the extremely low-total caloric, low-protein diets which were formerly advocated, now seem undesirable. In general, the patients who are definitely overweight in proportion to their height, as determined by some simple formula for the estimation of ideal weight, should be slowly reduced: (1) By a limitation of the total diet; and (2) by a sharp reduction of the fat component. Patients who are underweight, and in my experience they are almost as numerous as those who are overweight, despite the present-day impression, these patients should be built up by additions in the fat and carbohydrate components. It has been established by Benedict[6] and his co-workers, that diets of low total caloric value reduced the systolic blood-pressure, but when they were used over prolonged periods, the resulting undernutrition brought about a secondary anemia, and a diminished vitality. The patient, therefore, paid the price of a lessened efficiency, if the goal was reached by undernutrition.

The diet that I find the most satisfactory has the following characteristics: It is simple, well-balanced, contains no more protein than the actual needs of the patient (0.8 gm. to 1 gm. of protein per kilo of body weight), of sufficient caloric value for the energy requirements (2000 to 3000 calories per day), easily digestible, suitable to the powers of mastication of the individual, and is free from excess of meat extractives, condiments and salt.

The method of prescribing a diet based on the foregoing principles, is somewhat as follows: The articles of the diet and the amounts which are to be allowed for the total twenty-four hour period, are checked on a specially prepared diet card containing lists of all the ordinary foods and their proportion of protein, fat and carbohydrate. In this way fairly wide latitude in the choice of foods of approximately the same food value can be allowed. The method is so simple and practical, that the patient soon acquires a sufficient knowledge to use the diet card intelligently, with little supervision.

Sodium Chloride. The question of sodium chloride is the *bête noire* of the present day management of essential hypertension. The restriction of salt in nephritis with edema is a well-recognized procedure, first proposed by the French investigators, Widal and Javal,[7, 8] in 1903. In 1920, Allen[9] in this country, advised a rigid salt-free diet for some cases of essential hypertension. In this condition he found the chloride threshold was high, and he suggested

that, "These patients purchase their apparent efficiency of salt excretion at the price of an abnormally high-blood salt and an increased blood-pressure." On the basis of the findings in a limited series of hypertensive patients, notwithstanding certain clinical contraindications of chloride privation, Allen maintained that a rigid salt-free diet brought about a reduced blood-pressure, relieved subjective symptoms, diminished the danger of apoplexy and possibly checked the progress of the condition. In a recent paper,[10] he reaffirms the foregoing statements, and adds, "It is a scientific fact that a relation exists between the chlorides and vascular hypertension." Mosenthal,[11] Christian,[12] and others do not agree with Allen, nor have they succeeded in influencing the blood-pressure by salt restriction. During the past two years, in work in the Clinic and with private patients, I have used salt-poor diets, which contained approximately 2 to 3 gms. of salt per twenty-four hours. In many cases, remarkable symptomatic results were noted following the restriction of salt, particularly in the alleviation of the characteristic morning headache, so common in this condition. No effect, however, has been found on the blood-pressure, even after prolonged periods. It has been suggested that the reduction in the fluid intake and food consumption, which follows salt restriction, is connected with the relief of symptoms. The whole problem of salt metabolism awaits further investigation and until this is forthcoming, final judgment on the advisability of salt restriction in essential hypertension, had better be suspended.

Physiotherapy, Hydrotherapy, Electrotherapy, Massage. The bathing habits of patients, with early hypertension, need not be modified. Hydrotherapy is a valuable adjunct to diet restriction and exercise, in weight reduction cures, and may be utilized for this end.

It is generally accepted that the high frequency current will produce temporary reduction in the blood-pressure with an accompanying relief of symptoms. I have had no experience with its use, but I see no objection to its employment for the symptomatic benefit it may afford, provided its administration is carried out by physicians with the special knowledge which is necessary.

Massage is another measure of physiotherapy most useful in elderly patients with vascular changes.

Infection, Syphilis and Tobacco. In the preliminary survey of cases of essential hypertension, local foci of infection in all regions (teeth, tonsils, paranasal sinuses, and prostate, etc.), should be noted. Although no direct relationship has been established between focal infection and vascular hypertension, nevertheless, I believe these foci should be gradually and carefully eradicated. I have been lead to this opinion for two reasons; in the first place, it is urgent to maintain the general resistance of these patients; and in the second place, it is important to protect the cardio-vascular-renal system from added strain or damage from infection. Ophüls[13]

has recently pointed out the importance of the presence of chronic septic infections to injury of the arteries, and to the development of arteriosclerosis; however, no direct relationship has been proved between vascular hypertension and arteriosclerosis.

It is surprising how well these patients with vascular hypertension stand anesthesia and surgical trauma, particularly when a short period of preparation has preceded the surgical procedure.

Syphilis, as far as we know, plays little or no part in the production of essential hypertension, in spite of its well-known predilection to arterial damage. The incidence of syphilis is found to be exceptionally low in hypertensive statistics.

The use of tobacco is best greatly curtailed in all cases, but positively interdicted in those individuals who present evidence of especial hypersensitiveness to it, such as tachycardia and cardiac irregularities.

Drugs and Organotherapy. We have no drugs which directly influence the course of hypertension. Digitalis, to which I will refer more fully later, may be used effectively at times in the early cases, that are beginning to show circulatory strain. Short courses of this drug, combined with rest in bed, should not be withheld until the heart has decompensated.

Insomnia and nocturnal restlessness must be controlled, and I know of no better sedative for this purpose than one which is less commonly used now than formerly, I refer to chloral hydrate, whose action besides that of a central nervous system depressant, is an excellent vasodilator. In therapeutic doses, it is not a cardiac depressant, as is sometime thought. Fifteen to 20 gr. of this drug, taken with warm milk at bedtime, will usually assure the patient of a good night.

The nitrites, except for their use in the vascular emergencies that occur in hypertension, are of no value. Potassium iodide, except in cases with a suspected luetic infection, or advanced arteriosclerosis, is useless. Organotherapy, with the various endocrine products in essential hypertension, has no scientific basis.

The Management of the Advanced and the Late Stages. The advanced stage of essential hypertension is characterized by both subjective and objective findings. Symptoms have appeared and demonstratable physical changes are apparent in the cardiovascular system. Cardiac hypertrophy, thickened arteries, and an accentuated aortic second sound are almost always present. In spite of slight urinary findings the renal function remains comparatively good. The clinical picture at this stage of the process may remain indefinitely, *in statu quo*, and management requires no special measures beyond those outlined already for the early cases.

The Three Important Complications of Advanced Essential Hypertension. There are, however, three important complications that may arise at any time during this period; namely, circulatory insuffi-

ciency, threatened cerebral hemorrhage (a sudden rise of blood-pressure, the so-called hypertensive crisis), and gradual renal insufficiency accompanied by the symptoms of uremia. The serious nature of these complications demands prompt attention.

Management of the Myocardial Insufficiency Secondary to Long-standing Hypertension. The presence of a flagging myocardium will be no surprise to the physician in the well-studied case. Its management requires rest in bed, reduction in diet and fluid intake, and digitalis. The Karrell[14, 15] diet, or a modification of it, serves to reduce the food and fluids. Violent purging should be avoided and the bowels moved with one of the vegetable cathartics or by enema.

The Use of Digitalis. The use and action of digitalis in this condition deserves special consideration. In spite of the fact that myocardial insufficiency secondary to prolonged hypertension, is seldom of auricular fibrillation variety, digitalis is of great service.[16, 17] If the picture of chronic passive congestion of the viscera and edema has developed (the so-called high blood-pressure stasis complex, as Elliott[18] terms it), the action of digitalis, through a redistribution of the blood from the venous to the arterial side of the circulation, is often dramatic in its promptness. The common statement that a dangerous increase of blood-pressure follows the administration of digitalis, is a myth not founded on clinical facts. Eggleston[19] has shown that digitalis has little influence on the systolic blood-pressure in either way, that it tends to produce a significant reduction in the diastolic and more decidedly, to produce a material increase in the pulse-pressure.

In the presence of good kidneys,[20] the skilful use of short courses of diuretics, such as theocin, may be effective in increasing the eliminative activity of the kidney.

Venesection of 500 to 800 cc of blood should be considered, particularly in the cases where the circulatory apparatus appears to be primarily at fault, and the kidneys in a comparatively good condition.

Threatened Cerebral Hemorrhage and Renal Insufficiency with Uremia. Threatened cerebral hemorrhage requires complete rest, an ice-cap, vasodilators, sedatives and possibly lumbar puncture.

The progression of cases of essential hypertension to gradual renal insufficiency, with the retention of nitrogen, and eventually to the development of the picture of uremia, is no rare sequence of events. The management of this condition is beyond the scope of this paper and is more appropriately considered with the subject of chronic nephritis.

Summary. It appears that the management of individuals manifesting essential hypertension is best planned on broad lines, tentatively accepting the postulate that the process results from a disturbance of the cardiovascular mechanism incited by several

underlying conditions. Bad heredity, unhygienic living, excessive mental and physical strain, and infection, may all play a part. A régime for each case should be based on a careful study of the individual's daily life and habits. The readjustment of the manner of living should take into consideration the patient's work, food, exercise, recreation, interests, etc., and all obvious faults corrected. The large number of early cases observed in comparatively young people, offer an unusual opportunity in preventive medicine, since much can be accomplished by simple measures without enforcing a life of invalidism upon them. The fact that over half of all cases of essential hypertension eventually die of some form of circulatory disease, emphasizes the paramount importance of protecting the cardiovascular system from any unnecessary strain and supporting the heart as the emergencies arise.

BIBLIOGRAPHY.

1. Allbutt, C.: Diseases of the Arteries including Angina Pectoris, Macmillan Co. (New York and London), in two volumes, 1915.
2. Janeway, T. C.: Arch. Int. Med., 1913, **12**, 755.
3. Janeway, T. C.: Johns Hopkins Hosp. Bull., 1915, **26**, 341.
4. Janeway, T. C.: Am. Journ. Med. Sci., 1906, **131**, 772.
5. Camp, W.: A Handbook of Health, and How to Keep It, D. Appleton & Co. (New York and London), 1920.
6. Benedict, T. C. et al: Human Vitality and Efficiency under Prolonged Restricted Diet, Carnegie Institute, Washington, Pub. 280, 1919.
7. Widal, F. and Javal, A.: Jour. de physiol. et de path. gén., 1903, **5**, 1107.
8. Widal, F. and Javal, A.: Jour. de physiol. et de path. gén., 1903, **5**, 1123.
9. Allen: Jour. Am. Med. Assn., 1920, **74**, 652.
10. Allen: Med. Clin. N. A., 1922, **6**, 475.
11. Mosenthal, H. O.: Med. Clin. N. A., 1922, **5**, 1139.
12. Christian, H. A.: New York State Jour. Med., 1921, **21**, 292.
13. Ophüls, W.: Arteriosclerosis, Cardio-vascular Diseases, Stanford University Pub. (Calif.), 1921, p. 102.
14. Osborne, O. T.: Disturbances of the Heart, Am. Med. Assn. (2d Edition), 1916. (See page 211).
15. Goodman, E. H.: Arch. Int. Med., 1916, **17**, 809.
16. Janeway, T. C.: Arch. Int. Med., 1914, **13**, 361.
17. Robinson, G. C.: The Therapeutic Use of Digitalis, Medicine, vol. **1**, pp. 1–137. (See especially page 58).
18. Elliott, A. R.: Jour. Am. Med. Assn., 1921, **76**, 1467.
19. Eggleston, C.: Jour. Am. Med. Assn., 1917, **69**, 951.
20. Christian, H. A.: Med. Clin. N. A., 1921, **4**, 1639.

LEUKEMIA: REPORT OF AN ATYPICAL CASE.

By Benjamin Gutmann, M.D.,
New Brunswick, N. J.

Leukemia is a disease about which much has been written and about which there are still many perplexing problems. It is not a new disease, but, since it was first recognized by Hughes Bennett,

and Virchow in 1845, the cause has never been discovered. The similarity, especially in the acute form, to an infection has been noted many times, and is the theory most credited as to the cause, but, in spite of much painstaking work, as for example, that of Dr. John F. Anderson and others, no one has been able to correlate these conditions. Circulating malignant tumor and a blood condition, resulting from and connected with myeloma, are other theories.

Obscure as the etiology of this disease may be, the recognition of the usual typical case is comparatively easy, and the purpose of this paper is not a discussion of those types. Since Ehrlich's classification of the white cells, and with the introduction of polychrome stains, much has been learned in the way of differentiation and separation of this disease into varieties and types.

Mention is made in various text-books of atypical cases, referring more especially to those presenting elements and characteristics of both chief types, and variations in the total number of white cells found in different cases, particularly those with fewer total white cells than usual. The fact that a fair percentage of cases present elements of both types is now quite generally agreed. Also, that the predominance of one type or another, as well as the total number of white cells, varies with the stage of the disease is well known.

Within the last few years the term "leukopenic leukemia" has arisen. In this condition the total number of white cells may not vary much from the normal, may be either slightly increased or even fewer, and yet constitute one of the varieties of the disease under discussion, its recognition depending upon the presence of abnormal or immature cells or a disproportion between the normal cells, as well as the associated clinical symptoms and physical signs. The term "aleukemic leukemia" has also been applied to this variety. These terms, of course, must be considered arbitrary and, so far as I know, have not as yet found general usage.

I desire to report a case which, I think, will fall into this category, and which, also, had peculiarities that should make it of some interest. At the outset I wish to state that I followed the usual classification and terminology of white cells as I knew it at the time, being aware that methods have been introduced to differentiate immature or abnormal white cells from normal cells. I refer to the oxydase reaction. It has not been proved, nor is it generally recognized that this has an advantage over a good polychrome stain for this purpose. The predominating abnormal, or immature, white cell in the case to be presented is the myelocyte, and in this paper the term will be used to mean those cells of moderate to large-size containing an irregular oval, or indented nucleus with a moderate to large amount of cytoplasm containing granules. No attempt was made to differentiate myelogones and premyelocytes from myelocytes. The identification of these cells as myelocytes

was agreed upon by several men of far greater ability than the writer in such work, who were consultants.

With the addition of the above-mentioned oxydase reaction, there has been added by some a third type of leukemia, namely, monocytic; so-called because of the negative reaction with this stain of a large mononuclear cell occurring in abnormally large numbers in cases having other characteristics and manifestations of the disease. While it is possible that this may constitute a distinct variety, it can easily be seen how perplexities are being added in the study of this interesting condition, and the question arises in our minds whether we are not straining at gnats in attempting so finely to separate and classify phenomena in the blood, which will eventually prove to be only a syndrome of some common cause.

CASE REPORT.—The patient was a man, aged sixty-three years, whose family and past personal history are of no particular importance, except to state that his habits were always good. He was a moderate user of alcoholic beverages and he denied any venereal infection.

His illness had an insidious and indefinite onset, and consisted for the most part of a sense of exhaustion, and easily induced fatigue; abdominal discomfort of an indefinite nature, except for a fairly fixed pain in the left side in the splenic region; nausea after taking food, but no vomiting; eructations; pains in legs; sweats, which he described as "cold sweats," during the night, or early morning hours; severe headaches; soreness in the neck along the border of the sternocleidomastoid muscles. These symptoms had existed for two or three weeks prior to July 20, 1920, when the patient was first seen and examined.

Physical Examination. The patient was a well-developed and well-nourished man of late middle-age, with an expression of depression on his face. His cheeks were flushed, but his color was otherwise good. Head: Sclera were clear; pupils reacted equally and normally; patient was slightly deaf, and the specialist who treated this condition considered it of catarrhal origin with no local inflammation in the ear itself. Mouth: Tongue heavily furred by dark-brown coating; many teeth missing, those remaining apparently sound with evidence of recent dental work; throat showed a chronic pharyngitis; anterior nares normal. Neck: Along border of the sternocleidomastoid muscle there were many palpable nodes of varying size, apparently tender on pressure, which felt like enlarged lymphatic glands; thyroid was not palpable and there were no abnormal pulsations. Chest: Symmetrical, with equal expansion on both sides; heart showed no thrills; apex palpable in fifth interspace in nipple line, with the exception of a slight, soft, systolic murmur at the apex, the sounds were clear and of good quality and there were no abnormal accentuations Blood-pressure, 158

systolic. Lungs: Anteriorly, resonance and breath sounds normal; posteriorly there was impaired resonance with diminished breath sounds and increased tactile fremitus over the right lower lobe, suggesting an old thickening of pleura; there were many moist crackles at the left base, but no apparent change in resonance. Abdomen: Moderate tympanites; liver reached from upper border of sixth rib to just below costal border; spleen could just be felt on deep inspiration, the area of splenic dulness seemingly increased; no other organs palpable; no shifting dulness in the flanks. Legs showed no edema or varicosities; no enlargement of joints; palpable long bones were smooth; no glandular enlargements other than those mentioned above were felt.

Laboratory Results. The sputum was negative for tubercle bacilli; urine was negative chemically and microscopically, except for a very few pus cells (prostate); blood Wassermann, negative.

Blood examination, July 29, 1920: Blood count: Red cells, 4,580,000; hemoglobin, 85 per cent; color index, 1.1 per cent; no blast cells, poikilocytes nor anisocytosis. White cells, 11,000 per cm. Differential count: Number of cells counted, 200; polymorphonuclears, 36 per cent; transitionals, 11.5 per cent; lymphocytes, 24 per cent; large mononuclears, 7.5 per cent; eosinophiles, 1 per cent; mast cells, 0.5 per cent; myelocytes (neutrophilic), 29.5 per cent.

Progress and Subsequent Course. The patient continued under my immediate care from above date, July 29, 1920, until August 9, when he left this city for his summer home. During this period his temperature ranged from 97 to 100.7° F., with daily afternoon rise; pulse, 68 to 92; sweats in the early morning hours were of daily occurrence. Complaints about nausea, and abdominal discomfort became more persistent; the stools were offensive in odor; patient slept poorly, but was about the house part of the day, and occasionally took a short auto ride; exercise of any sort produced great fatigue, and there was occasionally slight dyspnea; pains in the legs and discomfort in the mouth persisted.

Diet, rectal irrigations and appropriate medication seemingly made no impression on the gastrointestinal symptoms.

August 4: A consultant from Philadelphia saw the patient, and agreed with the diagnosis. Further blood examinations at this time were in all essential respects similar to that recorded above. From August 9 to August 24 the patient was out of my immediate care, and under the care of a local physician at his country home. From the nurses' records, which were accurately kept, it appears that the patient grew gradually worse, so that more and more time was spent in bed. The tongue became the seat of actual ulcers; the gums were inflamed; the breath became fetid in odor; headaches were intense and persistent; the glands in the neck increased in size, and became more painful; the abdominal distress increased,

and on one occasion, August 19, he vomited mucus, which contained a fair amount of bright-red blood. At this time a rash appeared on his arms and legs, which afterward proved to be subcutaneous hemorrhage. The patient became delirious. His temperature during this period ranged from 97.6° to 102.3° F. The pulse was from 96 to 132, the temperature remaining elevated most of the time.

August 24: I was called hurriedly to see the patient with the statement that he was dying, and when I arrived I found him with a pulse that was absolutely irregular and uncountable, dyspneic, with great difficulty in swallowing, and covered with profuse cold perspiration; respiration, 32. His body was almost completely covered with large patches, bright red in color, due to subcutaneous hemorrhage. He looked, to all intents and purposes, to be in extremis. He responded to very vigorous stimulation, digitalin 1/25, intravenously every three hours for four doses, and the next day his pulse was 100 to 108, temperature 100° to 101.2° F. and respiration 28 to 32, having tided over what seemingly was a crisis. Stimulation in lesser doses was continued. From this period until September 17 the temperature very slowly subsided, and by the date mentioned became practically normal. The pulse remained rather rapid, usually 100 to 110, and respiration 28 to 36. The hemorrhagic areas gradually underwent resolution, but the digestive disturbances, ulcers in the mouth and headaches persisted. However, the mental symptoms became more and more troublesome. There was mental confusion, muttering often, hallucinations and delusions. These mental symptoms seemed to bear no relation to fever, persisting after the temperature became normal. The glands in the neck had decreased considerably in size during this period, and there was no change in the spleen and liver from that noted in the original examination.

September 25: The white-cell count was: Polymorphonuclears, 62 per cent; lymphocytes, 28 per cent; large mononuclears, 2 per cent; eosinophiles, 4 per cent; neutrophilic myelocytes, 3 per cent; transitionals, 1 per cent.

The mental symptoms persisted and followed no definite trend; the patient was disoriented and frequently rebellious, with hallucinations and delusions. He was often incontinent of urine and feces, and at times refused food, so that feeding became a difficult problem. Otherwise, the most annoying symptoms were the stomatitis and gingivitis. Sleeplessness was marked, and he resisted everything but morphin and hyoscin. The patient still complained of pains in his legs and digestive discomfort, and there was considerable foul-smelling flatus from bowel. His physical condition improved, and he was able to spend part of the day out of bed.

The persistence of the mental symptoms so long after improve-

ment in his physical condition caused much anxiety, and on October 28 Dr. Dercum, of Philadelphia, was called for conference. His opinion was that it was a psychosis due entirely to his disease, and that the prognosis was that of the disease underlying it. He had seen two other cases of like character.

November 4: The blood count was as follows: Red cells, 4,200,000; hemoglobin, 90 per cent. White cells, 5900; polymorphonuclears, 57 per cent; large lymphocytes, 7 per cent; small lymphocytes, 29 per cent; large mononuclears, 1 per cent; transitionals, 3 per cent; eosinophiles, 2 per cent; neutrophilic myelocytes, 1 per cent.

It will be seen that change in characteristics of the white cells had taken place; this was noted in other examinations not recorded here. There was a marked disease in the myelocytes, and a relative increase in lymphocytes, with no change in red cells. This relative lymphocytosis is further increased in a count made on December 18, 1920, which follows: White cells, 6450; polymorphonuclears, 51 per cent; small lymphocytes, 39 per cent; large lymphocytes, 4 per cent; transitionals, 2 per cent; eosinophiles, 2 per cent; neutrophilic myelocytes, 2 per cent. There were no blast cells, poikilocytosis or anisocytosis.

November 9: The patient was able to take an auto ride for the first time, although there was no radical change in his mental condition, and he still required morphin and hyoscin for sleeplessness. His temperature would occasionally reach 99.4 by rectum in the evening.

December 1: The patient was up and about considerably during the day, although he became fatigued very easily; his mind had improved and he recognized his surroundings. Morphin and hyoscin for sleep could be dispensed with.

December 11: The patient was able to take a short walk, and on December 13 he went to the office for the first time. He was still easily fatigued and complained of aching in legs and soreness in mouth, although ulcers in his mouth had completely healed. Improvement continued gradually, and the patient a few months later considered himself entirely well.

Subsequent blood counts were as follows:

January 13, 1921: White cells, 7800; polymorphonuclears, 56 per cent; small lymphocytes, 26 per cent; large lymphocytes, 9 per cent; mast cells, 1 per cent; neutrophilic myelocytes, 7 per cent; eosinophiles, 1 per cent. No blast cells, poikilocytosis or anisocytosis.

There is a slight increase in myelocytes from previous counts, but the relative lymphocytosis also persists.

May 11, 1921: Red cells, 4,340,000; hemoglobin, 85 per cent. White cells, 8700; polymorphonuclears, 57.5 per cent; small lymphocytes, 28 per cent; large lymphocytes, 11 per cent; neutrophilic myelocytes, 3.5 per cent.

September 25, 1921: White cells, 5750; polymorphonuclears, 55 per cent; small lymphocytes, 28 per cent; large lymphocytes, 7 per cent; large mononuclears, 4 per cent; transitionals, 4 per cent; neutrophilic myelocytes, 2 per cent. No nucleated reds.

June 15, 1922: Red cells, 4,850,000; hemoglobin, 90 per cent; no poikilocytosis nor anisocytosis. White cells, 5600; polymorphonuclears, 67 per cent; large lymphocytes, 6 per cent; small lymphocytes, 23 per cent; large mononuclears, none; transitionals, 3 per cent; eosinophiles, 1 per cent; basophiles, none; myelocytes, none. No nucleated red cells.

The treatment in the main was symptomatic. Large doses of red bone marrow and arsenic were given, but what effect this had, if any, I cannot say.

Summary. A case is reported with the following points of interest: 1. Many of the clinical signs and symptoms of an acute leukemia, with a high percentage of myelocytes in the beginning of his illness, with only a slight increase in the total number of white cells.

2. Gradual diminution in the number of myelocytes and slight relative lymphocytosis, with a return to approximately normal of the total number of white cells.

3. Relatively very slight disturbance of red cells and hemoglobin.

4. Occurrence of what might be termed a crisis, following which there was slow, but steady, improvement.

5. A marked psychosis considered to be a consequence of the disease.

6. A complete symptomatic recovery, both mental and physical.

7. Return of blood to normal, or nearly normal.

Conclusions. Notwithstanding the doubt in the minds of many physicians, the blood finding and clinical picture in this case, in my opinion, justify a diagnosis of leukemia of that type spoken of as leukopenic leukemia, and if this is accepted we have a rare instance of recovery from that disease.

THE RELATIONSHIP OF GOITER TO MENTAL DISORDERS.

By Harold L. Foss, M.D.,
SURGEON-IN-CHIEF OF THE GEISINGER MEMORIAL HOSPITAL,
AND
J. Allen Jackson, M.D.,
SUPERINTENDENT OF THE DANVILLE STATE HOSPITAL, DANVILLE, PA.

The study of the subject of goiter and its relation to nervous and mental disease has received a great deal attention as is shown by a review of the literature. Farrant[1] in a detailed study of the thyroids

in 1000 cases of insanity found the gland often "abnormal," varying from considerable enlargement with hyperthyroidism and exophthalmic goiter to complete atrophy with myxedema and cretinism and holds that disturbance of secretion, whether in the form of excess, deficiency or absence, causes an "altered mental state and this combined with the effect of various toxemias renders the patient insane or liable to insanity from slight mental stress." This is typical of the theories advanced by many writers who would link up the endocrine system and especially the thyroid with the insanities and do so, often quite dogmatically, yet fail to support their claims with convincing proof.

The relation of the thyroid and ovaries to confusional insanity has been considered at some length by Wright.[2] The author points out that "endocrine disturbance may be the cause of all insanities and probably also of psychoneuroses," and states he has "never seen a case of hysteria with a normal endocrine system," yet fails to show what is the normal or how it is to be determined.

The observations of Raymond and Serieux,[3] although made over thirty years ago, seem to us to be logical and sound. These authors, after studying a large number of patients in the French asylums, hold that the psychic disorders of Graves' disease are not specific and may assume any form; that they should be considered apart from the disease and be referred to the morbid process to which they properly belong. These authors feel that the occasional association of Graves' disease and mental degeneration is not always a mere coincidence but can be explained by the hereditary defects that give rise to both conditions.

Barker[4] calls our attention to the usual neurotic and psychic states seen in exophthalmic goiter, conditions which are familiar to all who see many patients with thyroid disease, and it is true that the state of anxiety-phobia, obsession, etc., are often the symptoms that cause the patient first to seek advice. We agree with Barker that pronounced maniacal and paranoid psychoses occur with thyroid disease, but they are rare and, as a rule, are seen only when there is a psychopathic heredity. A few years ago reports of thyroid disease in dementia precox led in many instances to partial removal of the gland but the procedure has never proven a permanent benefit in any large series of cases. It is the feeling of the authors that, with those patients presenting symptoms of dementia and having associated goiter, thyroidectomy is not indicated and if performed will merely precipitate the mental disturbance.

Hammes[5] in referring to the work of the English Myxedema Commission states that true psychosis is not uncommon in hypothyroidism, the Commission having found such states in 8 per cent of 109 cases examined. The mental symptoms are usually subacute, and, although melancholia predominates, they may take the form of mania.

McCord and Haynes[6] noted only 0.5 of 1 per cent of cases with thyroid hyperactivity in their study of the endocrine glands of the feeble-minded. Ramadier and Marchana studied the thyroid glands of the insane patients in a goiter district, not finding a greater incidence of cases among the insane than among the sane. From an extensive survey of a large number of cases in many State Hospitals for the Insane, Woodbury[7] believes "it safe to say that only a relatively small proportion of hyperthyroid cases actually become insane" and, following a study of 300 thyroid cases coming under his personal observation, states that "none presented any psychoneurotic symptoms of possible thyroid origin.

Massarotti[8] in an exhaustive study of the mental disturbances of Basedow's disease (a study covering 173 pages with bibliography of 435 references) arrives at the following conclusions:

"1. Every syndrome of Basedow's disease presents some nervous symptoms, varying from a simple restlessness, to mild melancholia, mild excitement and a tendency to assume a hostile attitude toward one's environment.

"2. Not infrequently the course of the disease is complicated by true psychoses the most common being melancholia and mania, but these disturbances rarely affect individuals not predisposed, and are generally observed in persons with nervous or mental heredity.

"3. There is no evidence of a pathogenic relationship between the psychoses of Basedow's disease and the disease itself. Generally the subjects are such as are seriously predisposed, most of them, in fact, give a history of previous mental disturbances in whom the trauma incident to Basedow's disease, emphasizes the existing defective nervous system.

"4. In most cases the patients have attacks of mania or melancholia prior to Basedow's disease, which, rather than causing new symptoms, arouses a latent condition."

The Survey at Danville. The authors feel that they are indeed fortunate in having available opportunities, data and facilities especially favorable for a comprehensive study of this subject.

Danville and its vicinity has long been known as a goiter belt. Situated in this field and in the same town there are two hospitals with two distinct classifications of usefulness. The State Hospital is devoted exclusively to the care of mental cases, while the George F. Geisinger Memorial Hospital is a general hospital. To each of these hospitals are admitted patients presenting many interesting types of goiter. The State Hospital offers excellent facilities for the study of goiter and its relation to the psychoses. The George F. Geisinger Memorial Hospital offers an opportunity for the study of the nervous manifestations associated with the many types of goiter in patients who are not mentally deranged.

Case Studies.—A review of the patients at the State Hospital revealed 59 cases of goiter in a total population of 1647. Of this

number 49 were females of the total census of 804 female patients, while there were 10 male patients in a total male population of 843.

In the study of the cases, an effort was made to determine: (1) The relationship between the beginning of the menses, first recognition of the goiter and the development of the mental condition in the female cases and the relationship of puberty, the time of the appearance of the goiter and the mental condition in the male cases; (2) the distribution of goiter among the various psychoses; (3) the types of psychoses to ascertain if possible the presence of a group of symptoms which might be noted in these cases as especially characteristic complications of goiter; (4) if thyroid dysfunction were present.

To determine the general relationship between the beginning of the menses, the goiter and the insanity, questionnaires were forwarded to the reference of each female patient. The replies to these were not satisfactory and the information taken as a whole was not very illuminating while in many instances no replies were received; some were returned unclaimed; many contained no information that would bear any relation on the appearance of these conditions; many stated when the menses began but no information was given as to when the goiter developed; four gave the ages when the goiter was noted, but contained no information relative to the menses; nine replies, however, contained some information which is tabulated as follows:

TABLE I.—AGE AT WHICH SIGNS APPEARED.

Menses.	Goiter.	Insanity.
15	30	30
15	49	From birth
16	Half grown	29
13	15	From birth
15	26	29
12	16	34
11	From childhood	42
14	20	28
15	Some time ago	26

In 4 cases the age when the goiter was first noticed, as well as the date of insanity, were given.

TABLE II.—AGE AT WHICH GOITER ANP INSANITY APPEARED IN FEMALES.

Goiter.	Insanity.
Over 30 years	From birth
Some years ago	40
55	55
49	39

In the male group the replies were as follows:

TABLE III.—AGE AT WHICH GOITER AND INSANITY APPEARED IN MALES.

Goiter noticed.	Insanity.
No definite date, but noticed prior to insanity	25–26
20	25
18	24
40	44
54	44
Not noticed	23–25
Not noticed	30
Not stated	43

Although the number is too small to draw any conclusions, the goiter when noticed in all cases, save 1, developed prior to the mental condition.

TABLE IV.—SUMMARY OF FEMALE GOITER CASES.

1. No. of Cases, 49.
2. *Classification of Psychoses:*

Manic depressive:		
Manic	9	
Depressed	6	17
Mixed	2	
Dementia precox:		
Hebephrenic	6	
Catatonic	4	12
Paranoid	2	
Epileptic psychoses		2
Psychosis with mental deficiency	7	
Mental deficiency without psychosis	7	14
Melancholia		2
Paresis		1
Psychosis with cerebral syphilis		1
Total		49

3. *Classification of Types of Goiter with Respect to Type of Psychoses:*

Manic depressive:	
All types	All cases of the adenomatous type
Dementia precox:	
Adenoma	10
Colloid	2
Epileptic psychosis:	
Colloid	2
Mental defectives:	
Adenoma	11
Colloid	3
Melancholia:	
Adenoma	2
Paresis:	
Adenoma	1
Psychosis with cerebral syphilis:	
Colloid	1

The adenomatous type of goiter predominates. Of the 49 cases, 41 are of this variety. None of the patients exhibited systemic evidences of toxemia and no goiters were of the hyperplastic type of true Graves' disease.

TABLE V.—SUMMARY OF MALE GOITER CASES.

1. No. of cases, 10.
2. *Classification of Psychoses:*

Manic depressive:		
Manic	2	
Depressed	1	3
Dementia precox:		
Hebephrenic	4	
Paranoid	1	5
Psychosis with mental deficiency		2
Total		10

3. *Classification of Types of Goiter with Respect to Psychoses:*

Manic depressive:	
All types	All cases of the adenomatous type
Dementia precox:	
Colloid	4
Adenoma	1
Mental defectives	All of the adenomatous type.

In but 1 case was there any evidence of goiter in the ancestry. None exhibited evidences of hyperthyroidism nor were any of the goiters of the hyperplastic type.

Distribution of Goiter to the Psychoses. Tables IV and V summarize the types of psychoses as well as the types of goiter found. Of the 49 female cases studied, 17 represented the manic-depressive group (manic 9, depressed 6, mixed 2); dementia precox 12 (hebephrenic 6, catatonic 4, paranoid 2); epileptic psychosis 2; psychosis with mental deficiency 7, mental deficiency without psychosis 7 or a total of 14 in the defective group; melancholia involution 2; paresis 1 and psychosis with cerebral syphilis 1.

It should be noted in these tables that goiter was most frequent in the manic-depressive group and in those suffering from dementia precox and mental deficiency. The value of this fact is lessened, however, when we consider that these groups represent the highest percentage of the population of any mental hospital. Nevertheless, it is interesting to note the absence of goiter in the senile psychoses and the low percentage in the epileptic psychoses, both of which represent also a rather high percentage of the hospital population.

In this group of 49 female cases, the adenomatous type of goiter was found in all the manic-depressives; dementia precox shows: adenoma 10, colloid 2; epileptic, colloid 2; mental defectives,

adenoma 11, colloid 3; melancholia involution, adenoma 2; paresis, adenoma 1; psychosis with cerebral syphilis, colloid 1.

The most striking feature is the prevalence of the adenomatous type in the manic-depressive group, in the dementia-precox group and in the mental-defective group, while the colloid type was noted in dementia precox, epileptic psychosis, and cerebral syphilis. It will be seen, therefore, that the adenomatous type of goiter predominates, of the 49 cases, 41 being of this variety. In the entire series of 49 patients there was no evidence of toxemia.

The summary of the male cases as shown in Table V is as follows: manic-depressive insanity is represented in 3 cases, dementia precox in 5 cases, psychosis with mental deficiency in 2 cases. Here again we note that the adenomatous type of goiter prevails in manic-depressive insanity. The colloid type, however, predominates in the dementia-precox group in contrast to the findings in the female cases while the mental defectives show the adenomatous type. Here again, we found a lack of symptoms of toxemia.

Study of the Mental Symptoms. A detailed study of the various types of psychoses, by Dr. H. V. Pike, Clinical and Community Director, shows that the mental symptoms presented in each group fall logically into a classification represented in the tables. The voluminous nature of the reports and the space required for their publication prohibit their presentation in this communication. In studying the cases every care was exercised to eliminate the possibility of error in diagnosis and to determine the possibility of the presence of mental symptoms which would tend to show a possible condition which might be called thyroid psychosis, or a psychosis with symptoms characteristic of thyroid disease. The clinical findings, however, were so distinctly characteristic of definitely recognized psychoses, each case falling into its proper classification, that the possibility of a mental clinical syndrome which might be regarded as characteristic of a psychosis associated with thyroid disease was ruled out. Neither were there any distinct physical findings indicating a general systemic disease associated with the enlarged thyroids of these patients.

Thyroid Dysfunction. Every effort was made by means of clinical studies, physical examinations and basal metabolic investigations to determine the presence or absence of thyroid dysfunction. With the means at our command, we were unable to find anything in this group of cases which would lead us to say that there was any marked evidence of disturbance of thyroid secretory function. We are led to believe, therefore, that the presence of thyroid enlargement can only be regarded as coincidental having no definite bearing on the mental disease from which the patients suffered.

The writers are not unmindful that, while the cases studied in detail in this presentation show no relationship between the thyroid and the mental disorder present, the general practitioner will fre-

quently find cases of exophthalmic goiter with certain associated neurotic or psychoneurotic manifestations. Such cases, however, do not represent a true psychosis.

It is interesting to note that at the State Hospital this type of patient, that is the neurotic or psychoneurotic patient with goiter, has not been admitted. The reason for this may be that these mental manifestations are due to toxemias which are modified by or cleared up under general hospital treatment. It would seem, therefore, that before we can associate any definite relationship between thyroid dysfunction and a true psychosis, we must have all the clinical symptoms associated with the psychosis, the definite clinical symptoms of thyroid dysfunction and a positive disturbance of the metabolic rate.

General Hospital Observations. It was important, in connection with this study, to make a survey of the various types of goiter that are constantly being admitted to the Geisinger Memorial Hospital, a general hospital, situated in the same town with the State Institution in which the mental cases of this series are being treated and drawing its patients from the same field. Both institutions are in a section of the country where endemic goiter is common and, while the hospital for the insane has among its 1700 inmates but 59 cases of goiter with an annual admission of not over 2 or 3 new cases, the general hospital has treated over 800 cases in seven years. Diffuse colloid goiters and the so-called "multiple adenomatous" goiter, either with or without hyperthyroidism, prevail with a certain percentage of true exophthalmic goiter. Many of the adenomatous forms are associated with thyrotoxicosis and advanced cardio-renal disease rendering this form one of the most important under treatment, not only numerically but also because of the advanced and serious nature of the complicating degenerative changes with which such patients are usually afflicted. Of the hundreds of patients admitted for surgical operation (and practically all other than patients with small colloid goiters are so treated) only an extremely small number have shown evidences of mental aberration. This has been especially true with the patients with the nodular forms of goiter and, even with patients suffering from the most profound toxemia of true exophthalmic goiter, although there may be nervousness and mild excitement, there has been very rarely true insanity. Large diffuse colloid goiters are occasionally seen in imbeciles, such conditions often being present among several of one family, but with these patients there has usually been an easily traceable hereditary taint and the goiter has existed merely as an accompaniment and surely not the cause of the mental inferiority. Occasionally patients with severe toxemia of exophthalmic goiter evidence a mild, transient, delirium but this has occurred with less than 1 per cent of our cases. Two patients among over 800 developed, several weeks after bilateral

resections, severe and uncontrollable mania with death ensuing. Both had been operated on for relief of large multiple adenomatous goiters without associated systemic symptoms, the type of gland necessitating extensive resection. The symptoms later developing surely were not those of a crisis of acute postoperative hyperthyroidism, nor did they in any degree resemble those of tetany. Many others among our patients have had as complete resections and have passed through an uncomplicated convalescence so that the cause of the grave results in the 2 cases mentioned has been a matter of conjecture with no satisfactory solution.

The neuroses of adolescence are frequently associated with diffuse colloid enlargements but that such mental states are the result of thyroid dysfunction is very improbable, and, surely in a section of the country where at least 15 per cent of the young girls have some thyroid hypertrophy, the two conditions can only be considered as coincidental and not as cause and effect. In the general hospital referred to, where the treatment of goiter is proving an important part of the daily work, no insane patients with goiter are being seen while mental disturbances developing in goiter patients under treatment are of the rarest occurrence and have been noted only in the occasional patients mentioned above.

Among the cases of insanity with associated goiter studied in this series at the State Hospital, there have been no examples of true exophthalmic goiter and while a few patients have shown evidences of mild hyperthyroidism as revealed especially by increased basal metabolic rates, the majority have presented no systemic evidences of toxemia. The incidence of the various types of goiter about parallels that of the patients with normal mentalities applying at the general hospital in the same locality, with multiple adenomatous goiter predominating with some diffuse colloids and with a small incidence of true exophthalmics.

So utterly futile has thyroidectomy in the insane cases seemed to be that but little tissue has been available for pathological study, but in the few glands that have been removed in the hope of aiding the patient, the nodular, so-called "adenomatous" forms with the various degenerative changes peculiar to goiter have been revealed and nothing further. Surely from what pathological studies that have been made, no connection between the thyroid as an etiological factor and the mental aberrations have been traceable. We have searched diligently among our insane for a case of definite hyperthyroidism, for, with such a condition present, much possibly could be promised by ligation and resection, but in this search we have been disappointed. It is, however, apparent to us, having under our observation constantly in the two institutions many hundreds of patients both normal mentally and insane, and both with and without associated thyroid disease, that there is no definite relationship between thyroid dysfunction and insanity. Treatment aimed at

the thyroid gland, therefore, with the hope of improving the mental state seems quite illogical.

It is too much to claim that there is a typical Basedow's psychosis. The mental state of the patient with exophthalmic goiter is of keen alertness, with mild excitement, but not insanity. "Restlessness and irritability are marked symptoms. The patients appear to be markedly stimulated and their movements are semi-purposeful, or even choreiform. Their mental outlook is self-confident and optimistic" (Plummer). Although the most advanced, untreated case may develop a preagonal mania, yet this is seen only as a terminal condition. Surely it cannot be said that the mental disturbances of exophthalmic goiter are specific, as is claimed by some authors. In the patients who present temporary mental disturbances, the latter do not differ from similar complications occurring in other exhausting conditions, such as tuberculosis, nephritis and similar diseases.

There has been a tendency of late to attribute any and all pathological states to disturbances in the organs of the endocrine system and so thyroid excision or thyroid feeding (it seems not to matter which) has been repeatedly urged in the treatment of the feeble-minded.

We believe that colloid goiter, especially endemic colloid goiter of adolescence, is at present passing through that phase of surgical exploitation through which most diseases seem to have to pass at one time or another. The honors which have been handed from the retroverted uterus to the appendix and from the latter organ to the movable kidney and ptosed stomach, are at present shared about equally between monkey glands and colloid goiter.

It is most deplorable that so large a number of unfortunate young people are being subjected to needless and harmful thyroidectomies. The patient who suffers from early psychic imbalance and has an associated colloid goiter is in grave danger when she falls into the hands of the loose thinker who is all too ready to attribute every abnormal state to disturbed thyroid activity. Among our patients in the State Hospital is one on whom one of us had refused to perform a thyroidectomy some years ago, even though pressed to it by the family. The patient at that time presented slight yet significant mental disturbances and possessed a small diffuse colloid goiter. Manifestly there was no connection between the two. A surgeon with large goiter experience later performed a thyroidectomy while in a few months the patient was committed as a clear-cut case of dementia precox.

Wright[2] has called our attention to the relationship of the thyroid and confusional insanity and melancholia and speaks of the changes taking place in the female after the menopause when the "Mental attitude reverts to a neutral type" when the "endocrines" especially the ovaries and thyroid play an important role. Yet much of

this is pure theory for at the present time no single problem of endocrine physiology has been satisfactorily worked out and the giving of thyroid and ovarian extract to middle-aged women with mental disturbances is but pure empiricism. The extremes to which the present vogue of endocrinology has carried many of us, urged on as we have been by the manufacturers of pharmaceuticals, have caused Marine in despair to speak of the new and struggling science as "endocriminology."

Basal Metabolism in the Insane. Ten patients taken at random although chosen from among those thought most likely to show evidences of hyperthyroidism, were referred to the Geisinger Memorial Hospital for basal metabolic determinations. The average results was + 6 although with 1 patient, on whom a satisfactory reading was obtained, a rate of + 26 was recorded. Many tests were unsatisfactory because of the patient's refusal to coöperate. One reading of + 50 was secured from a patient not definitely hyperthyroid, the high rate probably being influenced by the patient's keeping her legs moving rapidly during the entire test. The conclusion is drawn that hyperthyroidism did not exist except in possibly 2 per cent of all the cases and in these but to a very slight degree. The multiple adenomatous type of goiter predominated with an occasional single cyst and a few diffuse colloid goiters. No typical small, symmetrical, parenchymatous gland of true exophthalmic goiter was discovered. Some of the largest goiters we have seen have been noted in the insane and several patients in this series had such massive adenomatous and cystic enlargements that their possessors appeared to support their heads only with great difficulty. None were clinically hyperthyroid. The two largest goiters in the institution were in two middle-aged sisters, one of whom was operated upon for the relief of pressure. The patient recovered satisfactorily but no change in the mental condition was noted and she died several months later from pneumonia.

Conclusions. The close observation of about 800 goiter cases coming to a general hospital for treatment and the simultaneous study of 50 goiter patients among 1700 inmates of a large hospital for the insane, both institutions in the same locality and drawing their patients from the same territory, lead us to draw the following conclusions:

1. That goiter is not, even in a goiterous district, especially common in the insane, rather the reverse, for its incidence in the State Hospital at Danville, Pa., is but 3 per cent.

2. Conversely, insanity is extremely rare among the large number of goiter patients applying for treatment in a general hospital in the same locality, there being no cases of true insanity among the 800 patients studied, the only mental disturbance being in the form of a mild excitement or rarely slight and transient mania, this in but 2 cases.

3. There is, apparently, no definite relationship between goiter and insanity and surely nothing to indicate thyroidectomy in the treatment of the usual insane patient suffering from complicating goiter, unless for the relief of mechanical pressure. Operation, of course, may be indicated if there be accompanying evidences of true hyperthyroidism, but this latter condition is most rare.

4. Neither hyperthyroidism not hypothyroidism occurs, except very rarely, among the adult goiter patients of the Pennsylvania hospitals for the insane, the greatest number of goiters being of the so-called multiple adenomatous or nodular forms and unaccompanied by systemic disturbances.

BIBLIOGRAPHY.

1. Farrant, R.: The Causation and Cure of Certain Forms of Lunacy, Brit. Med. Jour., 1916, **1**, 882.
2. Wright, J. S.: The Relation of the Thyroid to Confusional Insanity and Melancholia, Kentucky Med. Jour., 1919, **17**, 271.
3. Raymond and Serieux: Troubles psychiques de la maladie de Basedow, abstract in Rev. internat. de bibl. méd., 1892, **11**, 294.
4. Barker, Lewellys F.: Nervous and Mental Symptoms in Exophthalmic Goiter, Med. Press and Circ., 1919, **107**, 85.
5. Hammes, E. M.: The Relation of the Internal Secretions to Neurology and Psychiatry, Journal-Lancet, 1916, **36**, 449.
6. McCord and Haynes: Dysfunction of the Internal Secretory System, New York Med. Jour., 1917, **105**, 583.
7. Woodbury, M. S.: The Psychoneurotic Syndrome of Hyperthyroidism, Jour. Nerv. and Ment. Dis., 1918, **47**, 40.
8. Massarotti, V.: I disturbi mentali nel morbo di Basedow, Roma, 1914.

A STUDY OF THE ULTRAVIOLET ABSORPTION SPECTRA OF CEREBROSPINAL FLUID—A NEW TEST.

(Preliminary Report)

By Takuji Shionoya, M.D.,
TOKIO, JAPAN.

(From the Research Laboratory of Prof. K. Miura's Clinic, Medical Department, Tokio Imperial University.)

A good many methods have hitherto been advocated for the examination of cerebrospinal fluid, but the one which depends upon absorption spectra of ultraviolet rays has never been introduced. I have, therefore, made a study of cerebrospinal fluid from patients suffering from cerebrospinal diseases and from control subjects, all being the in-patients of the medical clinic of Prof. K. Miura. This was carried out at the laboratory of Dr. Yuji Shibata, professor

of the College of Science of the Tokio Imperial University, with the coöperation of Prof. Shibata and Dr. T. Inouye, an assistant to the professor.

Theoretical and Experimental. The appliances necessary for the experiment are emission apparatus, Baly's absorption tube, and Adam-Hilger's quartz spectrograph.

Emission Apparatus. Iron gives an electric arc, lasting two or three hours, because of its high melting point. If the two poles of the electric arc are made of iron clubs, when a 100-volt, 4 to 5 ampère current is passed through the system the iron evaporates in the electric arc heated to incandescence. The white spark of this iron gives a photograph of a special, long, and densely arranged line spectrum. Since each wave length of these lines has been thoroughly explained, and also since iron is comparatively inexpensive, the use of iron is practical.

Baly's Absorption Tube and Quartz Spectrograph. In taking a photograph of absorption spectra, it is advisable to alter the thickness of the layer as long as the concentration of solvents does not exceed a certain degree, rather than to change the concentration of solution each time. For this purpose, Baly's absorption tube is commonly used. The apparatus is constructed of outer and inner glass tubes; the inner tube is inserted in the outer one by means of a gum stopper. The layer can be changed by regulating the inner tube. There is a globular attachment on the top of the outer tube in order to hold the excess of fluid, and a scale on the side indicates the thickness of the layer. Quartz plates pasted on the end of both tubes give forth the spectra about 20 cm. in length, spreading from red to ultraviolet. The fluid to be examined is put into the upper attachment and the inner tube is regulated so as to change the thickness of the layer from 10 cm. to 0.1 cm. Of Baly's various tubes, one 10 cm. in length and 10 cc in capacity is used. It is attached to Adam-Hilger's quartz spectrograph, and by moving the film up and down, a photograph of each spectrum in each layer can be taken on one film.

Quantity of Cerebrospinal Fluid. The quantity needed for this examination is not more than 10 cc, this being the capacity of the tube. Strictly speaking, 8 cc of fluid is found to be sufficient, because in normal fluid the absorption appears in the thickness of 8 cc, and in abnormal, less than 8 cc.

Concentration of Cerebrospinal Fluid. The dilution of the cerebrospinal fluid is not necessary.

Drawing of Absorption Curve. In general, when there are some solvents which absorb ultraviolet rays, the absorption appears as a wide band on the spectrum. By Beer's law,[1] the width of the band changes according to the concentration of solution or the thickness of the layer. When the concentration or the layer is increased, the band becomes wider, and when they decrease, it

becomes narrower, and at a certain point, disappears. This fact enables us to judge the density of the solvents. The location of the absorption would also tell the molecular structure of solvents. In order to know them we have to draw the absorption curve. The

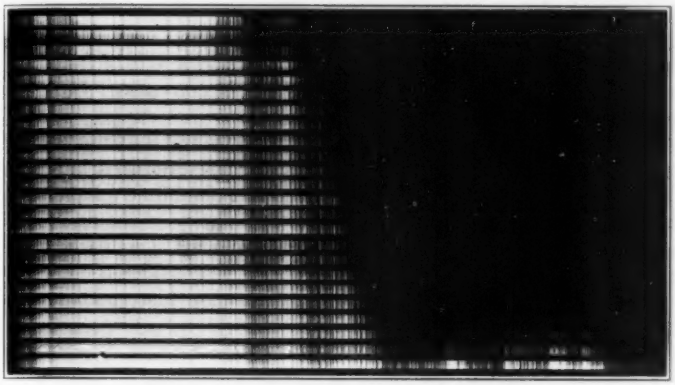


FIG. 1

method of drawing the curve was first introduced by Hartley.[2] He took a photograph of absorption spectra in various thicknesses of layers, and measured the wave length of the absorption end under the microscope. Taking the wave lengths of the absorption ends as abscissæ, and the widths of layers or concentrations as

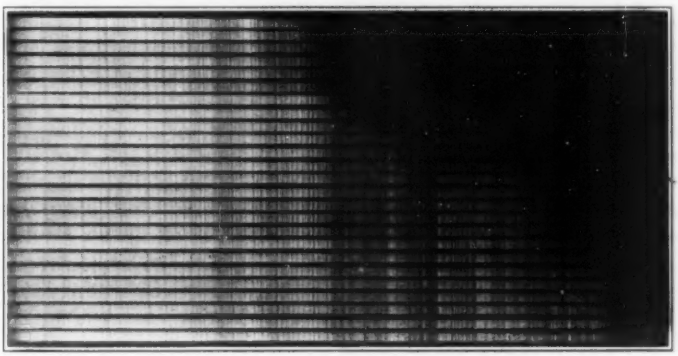


FIG. 2

ordinates, the curve was drawn. This method, however, is not satisfactory because, when the thinnest layer at which the absorption is produced becomes less than 1 cm., the curve would not show the difference of layers. On this account, even if there is the absorption

band, the basis of absorption curve becomes extremely flat and it is difficult to find the center of the absorption band. When the logarithms of the thickness of layers are taken as ordinates instead of the thickness itself, as Hartley later modified the method, the curves shorten at the thick layer in width and elongate at the thin layer, and the variation becomes apparent. When the reverse (it is called wave number) of wave length is taken as the abscissa, instead of wave length, the red ray appears to the left of the ultra-violet, as is seen in ordinal spectrum and is convenient for comparative study.

The cerebrospinal fluid subjected to the above test does not change its chemical composition, neither is the quantity reduced. Therefore, assisted by other known tests of cerebrospinal fluid I have been able to carry out my tests with a limited quantity of the fluid.

History and Pathological Findings of Patients. Ten cases were examined and studied, except two which were considered clinically normal in the cerebrospinal system. The case histories were as follows:

CASE I.—S. K., farmer's wife, aged thirty-one years.

Previous History. Had been healthy, had suffered from no noteworthy sickness, one normal parturition, no venereal diseases.

Present Status. No pathological alterations in internal organs, nervous system, or skin. Wassermann test negative, diagnosed as healthy. On July 20, 10 cc of cerebrospinal fluid was taken.

CASE II.—I. I., farmer's wife, aged thirty years.

Diagnosis. Graves' disease, with apical infiltration of right lung.

Previous History. From the early part of February, 1922, had complained of tired feeling in whole body, palpitation, thirst, and sweating, etc. No venereal diseases. In the middle of February, struma was discovered by a physician. Had had three abortions, and two babies died immediately after birth.

Present Status. Slight exophthalmos, symptoms of Moebius, von Graefe, Joffroy, etc., present. Boston's and Stellwag's symptoms absent. Thyroid gland enlarged, with murmur heard on auscultation. Heart enlarged on both sides; heart-sounds strong, impure; systolic murmurs over heart. Marked tremor of hands. Wassermann reaction of serum positive. Dulness at apex of right lung. On May 19, lumbar puncture performed.

CASE III.—T. M., dealer in pouches, aged forty-four years.

Diagnosis. Tabes dorsalis.

Previous History. When about twenty years of age, suffered from bubo on right side. On February 25, 1922, was run over by an automobile, occiput injured, unconscious for about five minutes. After two or three days felt headache and had paresthesia and

hypesthesia in both hands and fingers. After twenty days, paresthesia noted in planta and toes, and ataxia in walking.

Present Status. Both pupils irregular, reflex to light sluggish, nystagmus present. Ataxia in both hands and feet. Test for Romberg's sign, positive. Internal organs show nothing abnormal. On May 25, lumbar puncture performed.

Three Cases of Spinal Syphilis. CASE IV.—K. K., employe of firm, aged thirty years.

Previous History. Twenty-one years ago suffered from gonorrhea. Though ignorant of being contaminated with syphilis, had had alopecia eight years previously, and when examined three years ago Wassermann reaction was said to be positive. Had had eight arsphenamine injections. His wife had had three abortions. Present ailment dated back to February of this year, when his feet became paretic and walking tremulous. He displayed paresthesia and hypesthesia first in right hand and then in left. These conditions were most marked at the beginning of April but subsided about two weeks later.

Present Status. Facial nerve, vision, auditory organs, etc., apparently normal. Pupils circular, light reflex present. Right foot slightly atrophic. Dorsiflexion of toes, incapable. Negative to Romberg's sign; no ataxia. Periosteal and tendon reflexes of limbs exaggerated, the right being more marked than the left. Clonus of both sides. Tests for Babinski's and Mendel's reflexes, etc., negative. The region below the lower abdomen and radial sides of both hands and forearms hypesthetic. Wassermann test on serum positive. On June 29, lumbar puncture performed.

CASE V.—T. U., greengrocer, aged fifty-five years.

Previous History. When four years of age suffered from smallpox. Denied venereal diseases. Had six children, another dying immediately after birth. Present disease began eight years ago with pain in left hand, followed by paresthesia of right scapular region; two weeks later paresis appeared in left upper extremity and gradually extended to the right upper extremity. From the middle of December of the same year, paresis and hypesthesia were noticed in both feet. The following year he suffered from dull pain in thigh and from dysuria. He had received no specific treatment but had had spontaneous remissions.

Present Status. Cranial nerves show nothing of note. Right pupil normal; left sluggish in light reflex. Internal organs normal. Periosteal and tendon reflexes of upper extremities hyperactive. Knee-jerk and Achilles-tendon reflex hyperactive. Babinski's phenomenon positive. Sense of touch and pain diminished in the left upper arm. Slight ataxia. Paresis of bladder with a feeling of retention after the urination. Frequent urinations. May 27, lumbar puncture performed.

CASE VI.—N. O., employe of firm, aged forty-two years.

Previous History. In September, 1921, showed paresis of left hand, and a few weeks later, dull pain began in left elbow and shoulder, also paresthesia of left upper arm and left hand. In the middle of December, paresis and paresthesia of right hand, also edema of right hand and right upper arm. From January, 1922, on, paresis of both hands grew worse, and in the middle of February appeared in both feet. Paresthesia and pain in shoulders and loins became much worse. A month later, he became incapable of walking and had to go to bed. Since February there have been urinary disturbances. At the end of March, slight atrophy of both hands noted. Early in May, symptoms were spontaneously relieved and patient began to walk again with some assistance. Patient married at the age of thirty-two years, and had four children. Denied venereal diseases. Wife had had no abortions.

Present Status. Pupils normal. Vision, hearing, and facial nerves show no pathological changes. Alopecia. There is a stiffness in neck and consequently movement is restrained. Lymph-nodes in elbows and neck palpable. Internal organs free. Hyperhidrosis of forearms and fingers. Extreme atrophy of muscles. Paresis in upper extremities and a slight tremor of fingers. Tendon and periosteal reflexes of both hands not active. Spastic paresis in both feet. Walking is spastic, paretic, and next to impossible. Knee and Achilles reflexes extremely hyperactive. Ankle-clonus on both sides. Babinski and Mendel-Bechterew's phenomena positive. Wassermann reaction on serum positive. Course of disease: Since June 13, mercury and iodin treatment. On June 19, became much better and was able to walk without assistance. Dysuria and hyperhidrosis disappeared. Cerebrospinal fluid was xanthochromic.

A Case of Brain Tumor. CASE VII.—S. M., cake-dealer's wife, aged thirty-eight years.

Previous History. Married at the age of twenty-two years, and had four children. One child died immediately after birth, and another died of meningitis when five years old. No history of venereal diseases. Grandparents died of tuberculosis and mother of gastric cancer. Present disease began in April, 1921, with difficulty in hearing, and pain in left ear. In September she had seizures of circumscribed headache first in right occipital region, later in left parietal and temporal regions. These seizures lasted for about two hours and would subside after yellow fluid was vomited. At first the seizure occurred once a month but since January, once every four days, at which time paresis started in the lower extremities. In February had frequent attacks of vertigo. Since the onset of the present disease there had been attacks of extreme pain in the left eye and the vision was disturbed. The

disturbance of vision gradually increased, becoming more intensive after every attack. In April, the visual field of the left eye was markedly narrowed, the upper and lower sphere being retracted.

Present Status. Temperature 36.8° C, pulse 70 to 80. No ptosis of eyelids. Paresis of left facial nerve. The corneal and conjunctival reflexes on left side abolished, and there is hypesthesia. Nystagmus present in both eyes. The left pupil indented and not circular and sluggish in light reflex. Vision: right 0.1, left 0.04. Both fundi show papillary congestion. Diminution of sense of touch and pain in the left half of face and mucous membrane. Olfactory sense lost in left. The sense of taste lost in the anterior two-thirds of the left half of tongue. The left ear-drum apparently normal but hearing disturbed. The bone conduction is extremely interrupted. Internal organs show nothing of note. The tendon and periosteal reflexes of extremities active, especially on left side. No Babinski's and Mendel-Bechterew's phenomena. Ataxia indefinite. Adiadochokinesis positive on the left hand. Wassermann test of serum negative. In spite of the negative Wassermann and possibilities of brain tumor, cerebrospinal syphilis was considered because of the extensive focal symptoms. Antiluetic treatment was given for a month without appreciable effects. In July the vision was invaded; amaurosis in the left eye, the right being capable only of counting fingers at close range. On June 15, cerebrospinal fluid was taken, which was xanthochromic and markedly positive in protein reaction. Spinal Wassermann negative. Accordingly the diagnosis of brain tumor is more probable.

A Case of Ischiatic Neuritis. CASE VIII.—Y. N., government official, aged forty-seven years.

Previous History. He did not remember having suffered from venereal diseases, but Wassermann test made eleven years ago was said to be positive. Ten years ago, had had sore throat and falling hair. In February, 1921, complained of tenderness along the right ischiatic nerve but in a month became a little better, due to medical treatment. At that time there was hypesthesia of the right toes. In October had a recurrence of the neuralgia, which in twenty days became very mild. In the middle of February of this year had dull pain along the left ischiatic nerve. In March this increased in intensity and extended down to the sole of the foot along the course of the ischiatic nerve.

Present Status. Pupils, vision, hearing, normal. Lymph-nodes not enlarged. Patellar and Achilles-tendon reflexes active. Slight tenderness of ischiatic nerves on pressure. Romberg's symptom positive. Gait slightly ataxic. There is hypesthesia in the median and posterior aspects of the left upper thigh. Wassermann test of serum markedly positive. On April 20, lumbar puncture performed.

A Case of Tuberculous Meningitis. CASE IX.—S. S., student, aged seventeen years.

Previous History. On February 9, 1922, had chill and fever. Had dry cough and headache with continuous high temperature. In March, felt as if oppressed on left breast. The patient showed symptoms of apical catarrh of right lung and pleuritis. From April 26, had attacks of headache and vomiting with diarrhea. In June, the headache subsided, nausea and vomiting still continuing. In the middle of June speech disturbance noted.

Present Status. On April 16, consciousness clouded and became lethargic. Pulse 90 per minute. Nystagmus present. Mydriasis in pupils. Lips dry, tongue coated. Movement of tongue disturbed. Marked stiff neck. Cervical glands enlarged to the size of a kidney bean. Thorax is flat and there is dulness in the right supraclavicular space over which respiratory sounds are weak. Pleuritic condition observed in the inferior and posterior parts of the right thorax, there being slight incurvature and rigidness of abdomen. Upper extremities show some resistance to the passive movements. Clonic movements of fingers. Fibrillary twitching marked in toes and calf. Knee and Achilles-tendon reflexes not particularly active. Kernig's phenomenon positive, Babinski's and Mendel-Bechterew's signs negative. On June 19 lumbar puncture performed. Patient died.

A Case of Epidemic Encephalitis with Kakké. CASE X.—K. G., farmer's wife, aged twenty-eight years.

Previous History. Spring of 1918, patient lapsed into lethargic condition without any noticeable cause. She complained of murmur in the left ear; had difficulty in hearing, double vision, and was light-shy. Does not know whether she had fever or not. In autumn paresis appeared in both sides of forearm and hands. Had had salivation for two years. Winter, 1921, paresis appeared in both feet. No venereal diseases.

Present Status. Countenance lethargic and appears as if smiling. No fever. No nystagmus. The right pupil is larger than the left. Pupils round, with absence of reflex to light. Heart-sounds impure in apex, second pulmonary sound is active and duplicated. The body posture attains that of Parkinson's disease, body bending forward. Gait and other movements sluggish. Limbs resist passive movements, there being rigidity in all muscles. Babinski positive in the right. Knee and Achilles-tendon reflexes are abolished. Paresthesia and hypesthesia present in both legs and the back of feet. Slight trace of albumin and urobilin in urine. June 24, lumbar puncture.

Result of Examinations. CASE I. Pressure 95 mm.; cells 4. Pandy negative; the first phase of Nonne-Apelt's test negative;

Wassermann reaction negative. The absorption curve (Chart I) shows a slight concavity under the wave length 2924° A in the thick layer and is almost horizontal between 2757° A and 2525° A. This means that there is no marked special absorption in this case.

CASE II.—Pressure 110 mm.; cells 6. Pandy, Wassermann, and the first phase of Nonne-Apelt's test negative. The absorption curve (Chart I) shows an end absorption in the thick layer, the base of the curve being horizontal between 2757° A and 2525° A.

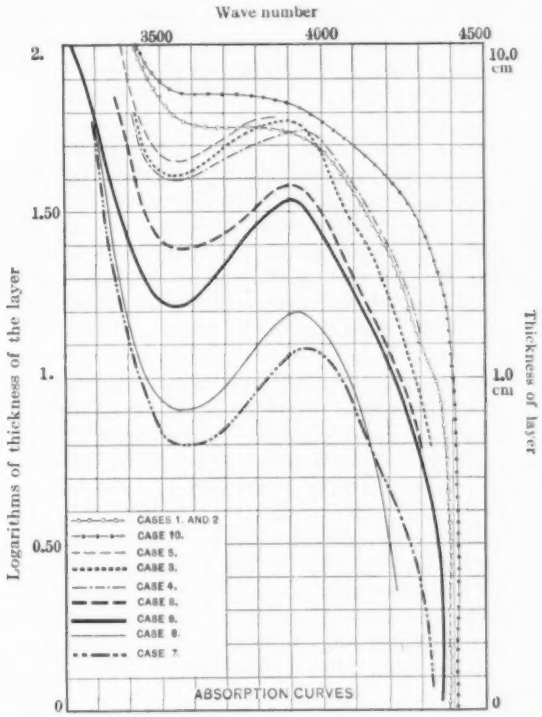


CHART I

These two cases are considered normal and the curves are almost the same. This type of curve is, therefore, designated as "normal curve."

CASE III.—Pressure 85; cells 6. Pandy and the first phase of Nonne-Apelt slightly positive; Wassermann test markedly positive. The special band absorption occurs between the wave length

2924° A and 2564° A, forming a decided valley. (Chart I.) The base of the valley falls in 4.0 cm. of the layer.

CASE IV.—Cells 28. Pandy and the first phase of Nonne-Apelt slightly positive; Wassermann negative. The absorption curve (Chart I) is similar to that of Case III, and a marked valley is shown between 2924° A and 2564° A, the bottom being in 4.0 cm. of the layer.

CASE V.—Pressure 120; cells 38. The first phase of Nonne-Apelt and Pandy slightly positive; Wassermann negative. The absorption curve (Chart I) duplicates those of Cases III and IV. The valley lies between 2924° A and 2564° A and the base in 4.5 cm. of the layer.

CASE VI.—The fluid is transparent but xanthochromic. Cells 8. The first phase of Nonne-Apelt, Pandy, and Wassermann all markedly positive. Hemoglobin negative by spectroscopical examination as well as in the spectrophotograph on panchromatic film. The valley of absorption curve (Chart I) is seen in the wave length between 2929° A and 2529° A and is so deep that the base of it reaches 0.8 cm. of the layer. This proves the existence of large amounts of absorbent substances.

CASE VII.—The fluid xanthochromic and transparent. Pressure 200. The first phase of Nonne-Apelt and Pandy strongly positive. Wassermann test negative. The valley of the absorption curve (Chart I) is the wave length between 2924° A and 2538° A, the base of it reaching 0.6 cm. of the layer.

CASE VIII.—Pressure 230; cells 12. First phase of Nonne-Apelt positive, Pandy markedly positive; Wassermann decidedly positive. The valley of the absorption curve (Chart I) is extremely deep, existing between the wave length 2924° A and 2564° A and the base is represented by 0.6 cm. of the layer. It is a well-known fact that the cerebrospinal fluid taken from patients suffering from ischiatic neuralgia contains more albumin than normal. In this case positive Wassermann and protein tests indicate a syphilitic process in the spinal meninges or in the nerve roots in addition to ischiatic neuritis.

CASE IX.—Pressure 440 mm.; cells 410, mostly lymphocytic with a few polynuclear leucocytes. Wassermann negative; Pandy and the first phase of Nonne-Apelt markedly positive. Cellular element removed by centrifuge and absorption spectra taken on supernatant fluid. The deep valley (Chart I) is formed between the wave length 2985° A and 2564° A and the basis in 1.6 cm. of the layer.

CASE X.—Pressure 120; cells 6. First phase of Nonne-Apelt, Pandy, and Wassermann reaction negative; Nylander's sugar test negative. The curve resembles the normal curve and the valley between 2857° A and 2632° A is nearly straight and lies in 7.0 cm. of the layer. (Chart I.)

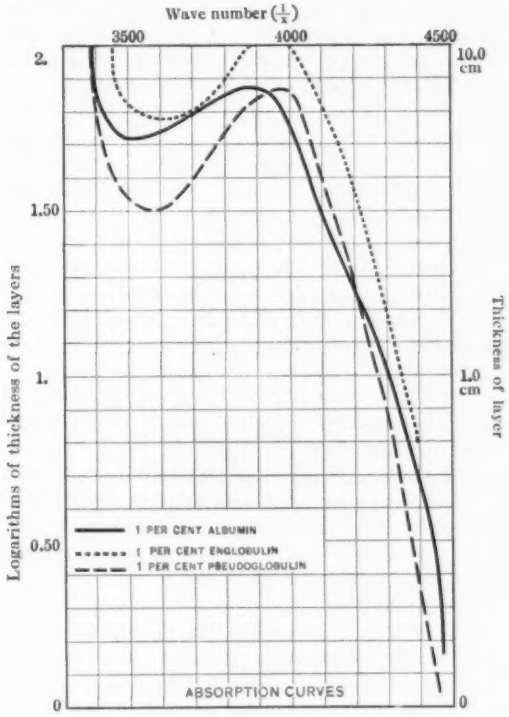


CHART II

Comment. From these results, it may be seen that the cerebrospinal fluid offers absorption on the spectrum of iron in the ultraviolet sphere nearly of the same wave length. The normal fluid presents a straight line, while abnormal fluids, except that of epidemic encephalitis, show a marked valley of absorption approximately between the wave length 2900° A and 2530° A. Although the thickness of layers which corresponds to the basis of valleys differs according to the density of the absorbing substances, the forms of the curves appear to be of the same type. The steepness of the curve, when compared with other tests of cerebrospinal fluid, does not correspond to that of the Wassermann test, but is parallel with that of protein tests, such as Nonne-Apelt and Pandy.

Thus it is presumable that the substance which gives rise to this curve is protein. What is the nature of the protein? Inorganic substances which absorb ultraviolet rays are complexes, and other colored salts and the simple salts have nothing to do with it. Organic substances have not been thoroughly studied in regard to this subject, although a little has been done on some proteins, uric acid, glucose, and dyes.[3 4 5] Urea does not show absorption by my own study. Soret and Hartley found absorption of glucose between 2220° A and 2150° A of the wave length respectively, while in my case it was shown in the wave length between 2900° A and 2530° A. Soret gives the absorption of globulin in the wave length 2900° A, of albumin in 2740° A; Hartley, of albumin between 2948° A and 2572° A, while Blyth claims that all protein substances would show absorption in nearly the same wave length.[6]

Recently (March, 1922) Lewis[7] has reported that three kinds of serum protein are practically the same with respect to the absorption curve. The writer has studied the absorption of ultraviolet rays on albumin, euglobulin, and psudoglobulin of horse serum, not having the report of the above worker at that time. Using 0.1 per cent of the solution, albumin has shown absorption in the wave lengths between 2941° A and 2584° A (basis 5.3 cm.), euglobulin between 2924° A and 2551° A (basis 6.0 cm.), and pseudoglobulin between 2941° A and 2538° A (basis 3.2 cm.). The absorption curves of these three proteins (Chart II) are much alike and are in remarkable accordance with the results of the last-named worker. The substances in the pathological fluid which have the property of absorbing ultraviolet rays are most probably protein bodies. But as to the exact nature of the protein the present study offers nothing very definite.

Conclusions. The author studied the absorption spectra of the cerebrospinal fluids taken from patients suffering from several kinds of diseases of the cerebrospinal system and plotted the absorption curves to compare it with that of normal fluid.

In the normal fluid the curve was shown with slight concavity between the wave lengths 2924° A and 2525° A in the thick layer, and was almost horizontal between 2757° A and 2525° A. This means that there is no special absorption band; this was designated as the "normal curve." The pathological specimen, except that of the epidemic encephalitis, manifested marked concavity in the same wave lengths (between 2924° A and 2520° A), the depth of the valley varying with the different diseases. The formation of the valley and its depth were proportional to the degree of the protein tests (Nonne-Apelt, Pandy) but not to the Wassermann reaction. The curve of epidemic encephalitis was practically the same as normal.

The serum albumin, euglobulin, and pseudoglobulin would show absorption in nearly the same wave lengths and the forms of their

curves and locations are in accordance with the pathological fluid. Therefore it may be presumed that the absorption spectra in the ultraviolet rays is due to protein. According to the depth of the valley, the concentration of protein can be roughly estimated. But as for the nature of the protein this study gives no definite information. The test can be applied together with the known tests for diagnostic purposes. It is more scientific than the usual tests which depend upon the intensity of cloudiness, insofar as this test expresses the quantity in the numerical manner. Another advantage lies in the fact that the fluid used for this can be subjected to other examinations without any change in either the quantity or quality of the fluid.

The writer is greatly indebted to the instruction of Dr. K. Miura, professor of internal medicine, Imperial University of Tokio, and to the valuable coöperation of Dr. Y. Shibata, professor of science, and his assistant, Dr. T. Inouye in completing this report. To these he wishes to express his deepest gratitude.

BIBLIOGRAPHY.

1. Beer, A.: Bestimmung der Absorption des roten Lichtes im farbigen Flüssigkeiten, Pogg. Ann., 1852, p. 86.
2. Hartley, W. N.: Researches on Spectrum Photography in Relation to New Method of Quantitative Chemical Analysis, Philadelphia Trans. 175, 1884, **1**, 49.
3. Soret: Kaysers Handbuch der Spectroskopie, vol. **4**.
4. Hartley, W. N.: Spectroscopic Notes on the Carbohydrates and Albuminoids from Grain, Trans. Chem. Soc., 1887, **51**, 58.
5. Blyth, W.: Ultraviolet Absorption Spectrum of Proteid in Relation to Tyrosine, Trans. Chem. Soc., 1899, **75**, 1162.
6. Soret, Hartley and Blyth: Loc. cit.
7. Lewis, J.: Ultraviolet Absorption Spectra and the Optical Rotation of the Proteins of Blood Sera, Proc. of the Royal Soc., Series B., 1922, **93**, 178.

REVIEWS.

LOCAL ANESTHESIA: ITS SCIENTIFIC BASES AND PRACTICAL USE. By PROF. DR. HENRICH BRAUN, Obermedizinalrat and Director of Kgl. Hospital at Zwickau, Germany. Translated and Edited by MALCOLM L. HARRIS, M.D., Professor of Surgery, Chicago Polyclinic; Chief Surgeon, Alexian Brothers Hospital; Surgeon to the Henrotin, Polyclinic and Passavant Hospitals, Chicago, Ill. Second American from the Sixth German (revised) Edition. Pp. 411; 231 illustrations. Philadelphia: Lea & Febiger, 1924.

THE first American translation from the third revised German edition in 1914, was one of the earliest works on local anesthesia to group and standardize these measures as we know them today. The present volume comprises the material of the former thoroughly revised with the addition of the newer ideas bringing it up to the present date. Various comments, throughout, are made by the American Editor. To Braun we owe the addition of adrenalin to our anesthetic equipment, this subject is therefore well worthy of our close study; it is presented in a style simple but masterly. Of interest among the additions is a toxic standard for novocain, a method of locating the various subcutaneous and deeper nerves before injection; a discourse on lumbar (spinal) anesthesia and sacral routes. Spinal anesthesia is treated in a manner which will undoubtedly give satisfaction in the majority of cases, but admits of one technic and, at most, two drugs. The percentage of failures is rather high according to our American standards, and in arriving at these figures no mention is made of the drug used, it is to be supposed that the ones mentioned in the text are the ones used. Chapter X on the advantages of local anesthesia and its particular uses make very helpful reading. A new route for injection of the trigeminal nerve is well written. Chapter XII, dealing with the neck, is entirely rewritten, while particular mention is made of the injection for operations on the thyroid and larynx. A graphic chart of the innervation of the thorax and its block anesthetic possibilities make of this subject a broad field of endeavor. Abdominal operative technic of local anesthesia are revised and thoroughly explained. Parasacral anesthesia is given a rightly important position and numerous heretofore difficult operative procedures under local are

made easily within the realm of the careful surgeon. A discussion of plexus anesthesia and its dangers to be avoided is handled well and methodically. The print in this edition is smaller and placed more close but the reading is easy and interesting. It is bound well and attractively. W.

MODERN UROLOGY. In Original Contributions by American Authors. Edited by HUGH CABOT, M.D., C.M.G., F.A.C.S., Dean and Professor of Surgery, Medical School, University of Michigan. Second edition. Two volumes. Pp. 1516; 686 illustrations and 19 colored plates. Philadelphia: Lea & Febiger, 1924.

ONE welcomes the appearance of a second edition of this most excellent and valuable work, representative of the best in American urology. Much has been accomplished in improving the first edition's mistakes and reduplications.

In Volume I is missed the interesting historical chapter by Watson, now deleted. The chapter on roentgenology is rewritten and with better illustrations. Corbus on syphilis now includes the subjects of luetic cystitis and the tabetic bladder; his chapter on genital ulcers presents the recent work on granulomas. Fowler includes Churchman's new operation for hypospadias and Young's for epispadias, while Ballinger has added a good word for acriflavine to his treatment of gonorrhea. Barney completely rewrites his splendid exposition of tuberculosis, and Hinman writes anew the chapter on testicular tumors as an authority that none question. Gardner also appears as a new collaborator and vastly improves the chapter on prostatic obstructions. On page 100, 4 per cent indigo-carmine solution is advised where a 0.4 per cent solution is certainly meant and was correct in the first edition.

Volume II on the whole shows less change. Peculiarly, Lower does not refer to Cullen's book on the umbilicus in dealing with vesical malformations; it would broaden his presentation. He rewrites the subject of diverticulum and presents his valuable work on exstrophy. Caulk includes just enough on Hunner's ulcers. Geraghty keeps apace with the times on the all-important subject of bladder neoplasms, and is now able to present some of his results with modern methods of treatment and the conclusions to be drawn therefrom; as may be likewise said of Young's chapter on prostatic carcinoma. The contributions of Keyes and of Cabot show very minor changes and the reviewer feels that many will agree with him that it is to be regretted that there is not more in the two volumes from the pens of these two most readable authors. The books appear in excellent sized volumes, handsomely edited.

R.

INTRA-NASAL SURGERY. By J. A. PRATT, M.D. Pp. 334; 195 illustrations. Philadelphia: F. A. Davis Company, 1924.

ONE is immediately impressed in reviewing this work with the clearness of text and the profusion of illustration. It first reviews the fundamental anatomy, physiology and pathology of the nasal cavity, and then includes among much miscellaneous material, special chapters on Atrophic Rhinitis, Submucous Septal Surgery, Development of the Lateral Wall, Turbinates, Ethmoidal Cells and Various Sinuses.

Nearly twenty full roentgen-ray plates are included in the book, with many working instruments *in situ* which concludes with a dozen coronal sections of the head, arranged in series. It is replete with suggestive points from practical experience, scarcely needed by the trained specialist; for him a more comprehensive description of the various sinus operations might be included.

While occasionally one might not entirely agree with the author's selective viewpoint, this work is however, a last word in the illustration of operative technic and a real contribution to literature.

B.

PRACTICAL CHEMICAL ANALYSIS OF BLOOD. By VICTOR CARYL MYERS, M.A., PH.D., Professor and Director of the Department of Biochemistry, New York Post-Graduate Medical School and Hospital. Second revised edition. Pp. 232; 33 illustrations. St. Louis: C. V. Mosby Company, 1924.

THIS new edition brings entirely up to date the subjects so well presented in the first edition. All the important blood determinations are here described carefully and in detail for the guidance of the laboratory worker. The significance and interpretation of these tests are properly evaluated for the clinician. There are also chapters on micromethods of urine analysis, on colorimeters, on standard solutions and reagents, and at the end of each chapter is an excellent bibliography.

F-H.

INTRAVENOUS THERAPY. By WALTON FOREST DUTTON, M.D., Medical Director, Polyclinic and Medico-Chirurgical Hospitals; Graduate School of Medicine, University of Pennsylvania. Pp. 542; 59 illustrations. Philadelphia: F. A. Davis Company, 1924.

THE first half of this book deals with the "General Technic of Intravenous Therapy" which is well presented. Unnecessary space

is devoted to certain matters, however, such as direct "artery to vein" transfusion. The second part of the book is a sort of medical compendium containing a list of apparently every disease for which anyone has ever recommended any form of intravenous medication. In each instance in addition to the suggestions for intravenous treatment is given an unnecessary "rehash" of the usual text-book symptoms, diagnostic points, and general methods of treatment. There is also an appendix containing tables of dosage, weights and measures, and tables of equivalents. F-H.

PEDIATRICS. By VARIOUS AUTHORS. Edited by ISAAC A. ABT, M.D., Professor of Diseases of Children. Northwestern University Medical School. In eight volumes. Volume I; 1240 pp. 284 illustrations. Volume II; 1025 pp.; 180 illustrations. Philadelphia: W. B. Saunders Company, 1923.

ENGLISH pediatric literature is rich in modern text-books and monographs, but no such comprehensive compilation as Abt's System has been published since Keating's "Encyclopedia" and "Supplement." In the quarter of a century intervening, the number of American and British investigators has been enormously increased and a vast amount of new knowledge has been acquired. A modern encyclopedia on children should be an inspiration to students, an aid to investigators, a boon to practitioners, and should be an incentive to a more scientific study of children in health and disease. Abt's Pediatrics will meet these needs. Most of the articles with their good bibliographies, are comprehensive enough to be of great value as works of reference; but in addition, the practical features are so clearly, logically and prominently presented, that they will appeal to the wearied practitioner.

The volumes consist of collections of monographs by a well-chosen list of authors. Although the Great War, and conditions following, delayed the publication of the work, most of the sections have been successfully revised or rewritten.

The first book contains a Survey of Encyclopedic Literature by Dr. Abt, a History of Pediatrics by Fielding H. Garrison, Congenital and Acquired Predisposition and Heredity by Clarence C. Little, a Summary of Anatomy by Richard E. Scammon, Growth and Development by T. Brailsford Robertson, Physiology of Metabolism by John R. Murlin, Application of Physical Chemistry to the Physiology of Childhood by Jesse F. McClendon, Hygiene of the School Age by Josephine E. Young, Hygiene of the Home, and Hygiene of Infants by Walter R. Ramsay, Climatotherapy by F. L. Wakeham, and Hygiene of Crippled Children by H. Winnett Orr.

Garrison's article is a fascinating and valuable résumé of facts

which, from primitive times, have had bearing on the development of the practice of pediatrics.

Of great scientific importance is the rather technical paper by Little. The statement that: "permanent racial improvement will come insofar as the germ plasma is improved, and no farther" may seem discouraging to many who are earnestly endeavoring to uplift the race by improving social and environmental conditions. The author, however, approves of such efforts, as they contribute to physical and mental progress, though they cannot alter the germ, but he would extend and amplify them. He makes a definite appeal to the medical profession to consider most seriously the question of human genetics in its relation to childhood and to racial development.

In the chapter on the anatomy of infants and children, much data from many sources is collected. The subject is of such importance, and is so well handled by Dr. Scammon, that more than 171 pages might advantageously have been given it. However, the superb bibliography chosen from about 5000 papers covers the subject completely.

Dr. Robertson throws new light on the question of growth and development, which will be of particular value to those interested in anthropometry. All persons responsible for the proper physical development of children should read this classic article.

The chapter on metabolism is most valuable. Dr. Murlin considers the metabolism of the newborn, the infant, and the child very completely under the title of Energy Metabolism. Under Substance Metabolism he goes into detail concerning the digestion, the absorption, and the intermediary metabolism of proteins and salts as they occur in the child. Discussion of the metabolism of fats and of carbohydrates is very brief, apparently due to the fact that protein and salts, constitute the "substrata of living protoplasm" and therefore concern metabolism most specifically. The bibliography covers the literature very well up to 1920 and contains some references as late as 1922.

The short lucid chapter on The Application of Physical Chemistry to the Physiology of Childhood will be greatly appreciated by many whose academic instruction in chemistry did not include electric conductivity, thermodynamics, hydrogen-ion concentration, etc.

Dr. Young has written an exhaustive article on the hygiene of the school child, that all physicians and school administrators should read. Every phase of child hygiene is considered fully; and much practical information is offered concerning posture, speech defects, exercise, sex hygiene and mental hygiene. School-health administration is also discussed at length.

The other chapters in Volume I are not sufficiently comprehensive for a reference book.

The second volume is comprised of sections on: Mortalities by

Richard Arthur Bolt, History-Taking Physical Examination by Mark Jampolis, Cerebrospinal Fluid, by Abraham Levinson, Roentgenology by Frederick C. Rodda, Peculiarities of Disease in Childhood by John Diven, Prophylaxis and Treatment by L. R. DeBuys, Heliotherapy by Henry Dietrich, Diseases of the Newborn by N. O. Pearce, Premature Infants by Julius H. Hess, Chemistry and Biology of Milk by Paul G. Heineman, Breast Feeding and Nutrition by Julius P. Sedgwick and Wyman G. C. Cole, Artificial Feeding of Infants by Joseph Brennemann, Diabetes Mellitus by Solomon Strouse, Diabetes Insipidus by Max Kahn, Seasickness by William J. Corcoran, Beriberi by Edward B. Vedder, Acidosis by John Howland and W. McKim Marriott, Obesity by T. C. Hempelmann, Infantile Scurvy (Barlow's Disease) by Alfred F. Hess, Pellagra by J. Ross Snyder, Rickets by Alfred F. Hess, The Constitutional Diathesis of Childhood by Frederic W. Schultz, and Acrodynia by William Weston.

Dr. Bolt's contribution is not an uninteresting statistical report on infant mortality, but an entertaining and instructive presentation of facts which prove the statement that "infant mortality can and should be largely prevented." The direct and contributing causes of infant mortality are discussed in a comprehensive manner, yet so clearly, that the reader wonders at the simplicity of the problem of prophylaxis, even though he appreciates the multiplicity of predisposing causes of disease. The author would solve the problem by education of the profession in medico-social pediatrics and in child-welfare work.

A chapter on Cerebrospinal Fluid summarizes the important facts concerning this fluid in a satisfactory and very convenient way. The editor and the author are to be congratulated for devoting a chapter to this subject.

Dr. Frederick C. Rodda discusses Roentgenology in reference to diseases of the lungs, pleura and mediastinum. So well is this phase of the subject presented, and so excellent are the illustrations, that one regrets the author did not also consider roentgenology in its relation to abnormalities of the gastro-intestinal tract and to bone diseases. However, these phases of the subject will probably be fully discussed later with the individual diseases. In fact, the finished articles on rickets and on scurvy in this volume, justify such expectation.

The section on Peculiarities of Disease in Childhood is especially valuable to those practitioners, who, not having made a special study of children, usually attempt to interpret the physical signs in infants and young children by comparison with normal standards for adults. Observation of the examination technic of the average hospital intern or of many general practitioners furnishes sufficient justification for such a chapter. Were Dr. Diven's article subdivided under various headings, its information would be more readily accessible.

The 83-page section on Prophylaxis and Treatment is chiefly a summary of methods of treatment. General treatment, care and nursing, aerotherapy, climatotherapy, dietotherapy, psychotherapy, therapeutic technic, hydrotherapy, electrotherapy, roentgen- and radiotherapy, and serum, vaccine and drug therapy are dealt with in 80 pages, including 25 pages which are devoted to a practical table of drugs and of dosage. Surely "prophylaxis" deserves more detailed consideration in an encyclopedia. Presumably the abridgment under this heading was due to a desire to avoid repetition, for several chapters in the preceding volume are devoted to various phases of prophylaxis. The chapter on Heliotherapy by Henry Dietrich is an interesting complement to DeBuy's treatise, but is not sufficiently comprehensive.

Two of the most noteworthy articles of this volume are Diseases of the Newborn by Dr. N. O. Pearce, and Premature Infants by Dr. Julius Hess. Both are so complete and practical that every physician interested in pediatrics, obstetrics, or public health, should read them.

Many practical points are found in the chapter on the chemistry and biology of milk. Following this, is the paper on breast feeding which summarizes the fundamental facts which every practitioner should have at hand.

The section on Artificial Feeding of Infants is a thorough, clear, simple, delightfully written exposition of the science and of the art of artificial feeding. It should do much toward removing the unfortunate and unwarranted mysticism that seems to surround the subject. Dr. Brennemann sanely appeals to the practitioner to master the few fundamental scientific facts concerning digestion, nutrition, elimination, etc., and to "know very definitely the behavior in the infantile economy of the different food elements, and the effect of modifying them so as to influence that behavior." This knowledge he truly claims may be acquired by "any intelligent graduate of medicine in a comparatively short time." He then urges the doctor to carefully and conscientiously study the baby and its environment and to apply his knowledge to the individual. The food should be adapted to the baby's needs, not to a prearranged table, not to meet a theory or "system." Perhaps few pediatrists will endorse all of Dr. Brennemann's conclusions and opinions, but his effort to bring the subject of infant feeding within the easy grasp of the family physician should meet with universal acclaim. For it is only through education of the doctor that the art of feeding will revert to him from the patent-food manufacturer.

The latter part of Volume II deals with definite diseases of children, all of which are very ably handled. It is surprising that in the discussion of diabetes only two paragraphs are given to the insulin treatment. Doctors Howland and Marriott have made a distinct contribution in their clear, concise discussion of acidosis.

Dr. Alfred Hess brings the subjects of scurvy and rickets up to date in two masterly monographs. The article on Pellagra is excellent, though it contains no reference to observations since 1917. The chapter on The Constitutional Diatheses of Childhood well repays careful perusal.

If the succeeding volumes are commensurate with these first two, Dr. Abt will creditably succeed in collecting "in monographic form the material which represents the fundamental knowledge of pediatrics" and will most probably attain his aspiration "to stimulate clinical and research work, especially by the younger men of English speaking countries." The compilation is so excellent that one regrets it has not been published in the loose-leaf form, so that revisions and additions might be readily made at short intervals of time. F.

FORTY-THREE GRAFTS FROM MONKEY TO MAN. By SERGE VORONOFF. Pp. 256; 38 illustrations. Paris: Doin, 1924.

THE author first gives the names of the surgeons who have used his method of grafting and then those who have assisted him in the operation. The list is too extensive to review. He gives as the indications for the operations the following: Absence of the testicle from castration, infantilism of the genital organs, orchitis following mumps, myopathies, chronic intoxications resulting in general asthenia, insufficiency of testicular secretion, neuresthenia, arteriosclerosis with premature senility, and senility with general debility. The results as given by the author are: Mortality, none, negative results, five (12 per cent). The latter were due to the use of an orchid from too young a chimpanzee. The positive results from the point of view of mental and physical improvement are given as 88 per cent (36 cases). Results from the point of view of mental, physical and sexual virility 65 per cent (26 cases). The age of the patients varied from twenty to seventy-six years.

The chimpanzee and cynocephale monkey being the nearest relations of the man were the only donors used. A graft made between two markedly distinct species undergoes necrosis rapidly. Minute researches as to the age of the "donor" have led to the conclusion that the monkey must have reached puberty or must be very near it.

The result of it all is indisputably favorable according to the author. Sexual power has, in many cases, not been restored which, according to the author, is a very small matter. The regaining of memory, the power to be able to "think and not feel tired," the general "young again" feeling were the main results which have encouraged the author in his work.

Although the author ascribes very little to the power of auto

suggestion, the reviewer believes this to be an important factor. Some of the illustrations appear to be convincing, but many are taken with varying backgrounds and intensities of the exposures. From the latter point of view, the reviewer feels that the pictures are inadequate and not convincing. Sixteen of his cases had gland transplantation for arteriosclerosis with general debility. It seems impossible to imagine an atheromatous vessel undergoing resolution and again taking on the characteristics of a normal one. It is but natural that the results seem more favorable to the expounder of the idea than to an unprejudiced critic. R.

WALTER REED AND YELLOW FEVER. By HOWARD A. KELLY, M.D. Third edition. Pp. 355; 15 illustrations. Baltimore: The Norman, Remington Company, 1923.

THE new edition has had certain minor additions made which have added but little to the value or interest of the book. The chapters which concern Walter Reed and his work are of intense interest but the added chapters concerning General Sternberg and General Gorgas, while perhaps rounding out the story do not seem as interesting or as well written. P.

EXCURSIONS INTO SURGICAL SUBJECTS. By JOHN B. DEAVER, M.D., ScD., LL.D., F.A.C.S., Emeritus Professor of Surgery; and STANLEY P. REIMANN, M.D., Assistant Professor of Experimental Pathology, University of Pennsylvania. Pp. 188; 30 illustrations. Philadelphia and London: W. B. Saunders Company, 1923.

THE volume comprises a group of lectures delivered by the senior author in July, 1922, at Washington University, Seattle, Wash., in the Extension Course for Graduate Physicians, also Dr. Deaver's address on the Centenary of Pasteur, an essay on Medical Education and Educators and a previously published paper on Living Pathology.

The lectures embrace peptic ulcer, jaundice, diseases of the bile passages and surgical conditions of the intestinal tract. The authoritative clinical views, based upon exceptionally rich experience, and the discussions of pathology, research and results of treatment, collaborating the work of an eminent surgeon and teacher with that of a brilliant pathologist and illustrating the invaluable coöperation between the amphitheatre and laboratory, make the kind of surgical literature that meets the requirements of the leaders of the profession as well as their progressive followers.

L.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

TAYLOR PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI,
CINCINNATI, OHIO.

The Staining of Treponema Pallidum in Dry Smears.—RUTH GILBERT and H. A. BARTELS (*Jour. Lab. and Clin. Med.*, 1924, **60**, 273) have prepared smears from the testicles of syphilitic rabbits. The presence of spirochetes has been demonstrated by dark-field illumination. The smears were divided into two sets, one of which was fixed immediately by heat, the other after an interval of four days (taking into consideration the time lost in transportation of specimens to a laboratory). The specimens were then stained and examined. The following staining methods were tried, 25 smears being stained by each method: Fontana, Tribondeau, Becker, Noguchi, Rosenberger and Fanz, Lipp, Ballenger, Medallia, Proca and Vasilescu, Oppenheim and Sachs, Reitman and Benian. One hundred and fifteen of the 375 smears examined were found positive. The following percentages of positives were found after staining with each of these methods: Fontana's method 80 per cent; Becker's method 60 per cent; Rosenberger and Fanz 28 per cent; and Lipp's method 24 per cent. The remaining methods were found to be useless. Seventy-five additional smears stained by Fontana's method gave 59 per cent positives. The morphology of *Treponema pallidum* in smears fixed after an interval of four days did not differ from that in smears fixed immediately. The technic used in Fontana's method was as follows: 1. Smears were air-dried and fixed with Huge's fluid (glacial acetic acid 1 cc; formalin 20 cc; and distilled water 100 cc) for one minute. 2. They were next washed in water, then covered with mordant of 5 per cent tannic acid, in 1 per cent carbolic acid solution, and heated until steam arose. The heated mordant was allowed to act thirty seconds. 3. Smears were rinsed quickly in water, blotted, and covered with a 2 per cent ammoniacal silver nitrate solution. (Ammonia should be added drop by drop

to the silver nitrate solution until a faint opalescence succeeds the brown precipitate first produced.) Heat was applied until steam arose and the heated stain was allowed to act thirty seconds. 4. The specimens were finally washed, blotted and examined.

Treatment of Myeloid Leukemia with Thorium X.—Ch. Aubertin (*Bull. et mém. Soc. méd. d. hôp., Paris*, 1924, **40**, 4) observed a considerable leukopenia (to 1500) in patients with chronic arthritis treated with thorium X; there was a modification of the leukocytic formula, consisting in polynucleosis and eosinophilia. These changes persisted during the course of the injections. There was no noteworthy change in the red count; nor was there any constitutional disturbance. In view of these facts, the author decided to try thorium X in the treatment of leukemia. A number of reports of its use in leukemia occurred during 1912–14, but since then, it seems to have been abandoned. The patient, a man aged fifty-five years, had been ill two months. He had a marked splenomegaly. Blood examination showed 2,850,000 red cells and 22,500 leukocytes, with 30 per cent myelocytes. Treatment was begun March 13, 1923 with subcutaneous injections of 300 micrograms; seven such injections were given at intervals of a week, then 400 micrograms and 200 micrograms were given. There was no local reaction, but each time the patient complained that they became painful. (He was an ambulatory patient, coming for the injection each week.) The treatments were discontinued May 16, the leukocyte count having fallen to 2700. Between June 29 and August 6 he had three roentgen-ray treatments. In August, all treatment was discontinued; leukocytes 1500, erythrocytes 1,460,00. The spleen was much decreased in size. November 25, the leukocyte count was still low, 3300. The red count, which had fallen to 1,670,000 June 16, rose to 2,870,000 in November.

Differential counts showed the following:

	Mar. 13, 1923, before treatment.	June 14, 1923, end of treatment.	Oct. 18, 1923, without treatment.
White count	22,500	2700	1500
Polynuclear neutrophiles	50.75%	64.0%	68.5%
Myelocytic neutrophiles	29.75%	13.0%	5.5%
Polymorphonuclear eosinophiles	2.00%	0.5%	2.0%
Myelocytic eosinophiles	1.25%	0.5%	2.0%
Polymorphonuclear basophiles	1.25%	0.5%	2.5%
Myelocytic basophiles	1.25%	0.5%	2.5%
Myeloblasts	1.50%	3.7%	5.0%
Lymphocytes	7.25%	14.0%	15.5%
Large mononuclears	6.25%	4.5%	6.5%
Normoblasts	1 to 400	3 to 200	3 to 200
Megaloblasts	2 to 400	3 to 200	3 to 200

The spleen showed little change in size during the course of the treatment, but later there was a steady decrease in size, which began sometime after treatment was discontinued.

An Analysis of the Clinical Histories of Patients with Pernicious Anemia in the Johns Hopkins Hospital from 1918 to 1922 Inclusive—C. R. Willson and F. R. Evans (*Bull. Johns Hopkins Hosp.*, 1924, **35**, 38) have analyzed the histories of 111 cases of pernicious anemia

and emphasize the following points: Pernicious anemia is about equally common in men and women and is a disease of adult life. It is never seen in children, is common in old age, and occurs most frequently between the ages of forty and sixty. It is very uncommon in negroes. The anemia once established, practically never regenerates. Anisocytosis and poikilocytosis are constant findings. Although a leukocytosis may occur in the presence of an infection, a leukopenia is the characteristic finding. An eosinophilia as high as 17 per cent may be found, but the increase is usually relative. The same applies to the large mononuclear and transitional cells. Myelocytes as high as 10 per cent may be found in an occasional case. Free hydrochloric acid in the gastric contents of these patients is so rare that, when present, it should put the diagnosis under suspicion. The spleen is palpable in only about 20 per cent of the patients. It may extend 5 or 6 cm. below the costal margin. The liver is palpable in about 33 per cent of cases. The edge may be palpated 5 or 6 cm. below the costal margin. All patients, whatever other discomforts they may have, suffer from one or more of the following symptoms: Weakness, disturbances of digestion, and nervous disorders of the extremities.

On the Phosphorus and Calcium of the Blood in Renal Disease.—O. L. V. DE WESSELOW (*Quart. Jour. Med.*, 1923, **16**, 341) reports a study of the phosphorus and calcium content of the blood in kidney disease and arrives at the following conclusions: A marked increase of the phosphate content of the blood in nephritis is of extremely grave import. The symptoms of uremia appear to show a close relationship to phosphate retention. On the average, retentions of phosphate and urea run a parallel course; the excretory mechanism of the two bodies is therefore probably the same. Independent variations in the retention of the two bodies are frequently observed, and are probably due to circumstances extraneous to the renal function. A diminished content of serum calcium is a bad omen, and appears to be connected with the generalized tremor and local twitchings of the final stages of uremia. No connection has been found between a diminution in the serum calcium and the generalized convulsions. The calcium-content of the serum in nephritis appears to show an inverse relationship to the content of inorganic phosphorus.

Bacteriological Observations on Acute Tonsillitis with Reference to Epidemiology and Susceptibility.—BLOOMFIELD and FELTY (*Arch. Int. Med.*, 1923, **32**, 483) used as material for their observations a group of about 200 young women, whom they were able to control as regards cultures, contact, etc. All cases of acute follicular tonsillitis were found to be due to hemolytic streptococci of the beta type. The organism may persist indefinitely in the tonsil, but rapidly dies out on the free mucous membranes. Carriers almost universally failed to develop the infection. There was an absence of demonstrable contact between successive or coincident cases. Evidence is adduced to show that the outbreak studied consisted of multiple instances of sporadic infection. There was a much higher incidence of the disease among individuals still possessing their tonsils. Of 104 persons with tonsils remaining,

41 were carriers of beta hemolytic streptococci, 63 were non-carriers. One individual of the 41 developed tonsillitis; 26 of the 63 developed the infection. Of the non-tonsillectomized, non-carriers who developed tonsillitis, a large proportion gave a history of previous tonsillitis. Their observations indicate that if a person reaches twenty years without having had tonsillitis, he has relatively slight chance of acquiring the infection.

Gonorrheal Myelitis.—PHIFER and FORSTER (*Arch. Int. Med.*, 1923, **32**, 530) point out the rarity of myelitis due to the gonococcus and give a bibliography of the 29 reported cases. The authors add 2 instances. One individual developed myelitis in the course of an acute gonorrhea, the other in a chronic urethritis. In most of the reported cases, the gonorrhea was said to be chronic. One patient died; 1 recovered completely. Of the cases on record, there was a death-rate of about 25 per cent. The endocardium is relatively seldom involved. The symptoms are those common to a myelitis from any cause. In neither of the authors' cases was the gonococcus recovered from the spinal fluid, but the etiological responsibility of this organism seems to be fairly clear.

Two Cases of Canine Tuberculosis Caused by Human Tubercle Bacilli.—PANISSET and VERGE (*Compt. rend. Soc. de biol.*, 1924, **90**, 341) investigated the origin of the tubercle bacilli in two dogs suffering with pulmonary tuberculosis with cavitation and rather marked hypertrophic osteo-arthropathy. They inoculated Petroff's medium with pus from the cavities according to the method of Limousin (*Ann. de l'Inst. Pasteur*, 1921, p. 558). Direct smears of the pus contained numerous acid-fast bacilli. After three weeks' incubation, several tubes gave a pure culture of tubercle bacilli. Several colonies were removed and dried between sterile filter papers; $\frac{1}{100}$ mg. of bacilli were injected into the ear vein of young rabbits, according to the method of Park and Krumwiede. Autopsies six months later showed a disseminated tuberculosis in 3 of 4 animals. The tubercles were found in the lungs, kidneys and a few in the liver, and were in various stages of evolution; they contained tubercle bacilli. These observations indicate the danger to human beings from contact with tuberculous dogs.

Local Vaccination of the Intestine Against Dysentery.—ANGLADE (*Compt. rend. Soc. de biol.*, 1924, **90**, 395) encountered an epidemic of bacillary dysentery in July, 1923, in the Garrison of Versailles, affecting chiefly the troops of Camp de Satory. There were also many cases among civilians. The first 3 cases were rapidly fatal, death ensuing in three to four days. An attempt at antidysenteric vaccination by means of oral administration, using the procedure of Besredka, was decided upon. There were 1132 soldiers in the camp. Of these 546 were vaccinated and 42 or 7.6 per cent developed dysentery; 586 were not vaccinated and 235 or 40 per cent of them contracted dysentery. Among the vaccinated it was learned that several retained the tablets in the mouth and expectorated them later.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Treatment of Hypertrophic Pyloric Stenosis.—POYNTON and HIGGINS (*Lancet*, 1924, **206**, 235) declare that the essential step in successful result is the surgical procedure. When once the diagnosis has been made operate at the earliest opportunity. Tumors were in all cases felt. Their method of examination was described in full. The difficult tumors are those lying high up under the edge of the liver, but they can usually be detected on inspiration by their harder consistence. The great hindrance to a successful result has been the duration of the symptoms. A strong infant with a long history of starvation is more likely to succumb than a weakly one with a recent history. Preoperative treatment and operation, which consists in division of sphincter, with refinements in controlling hemorrhage, are described.

Surgical Treatment of Unilateral Pulmonary Tuberculosis.—ARCHIBOLD (*Am. Jour. Surg.*, 1924, **37**, 17) states that the evidence of resistance is the prime essential and in this particular the help of the expert in tuberculosis is necessary. Fever, rapid pulse, large amounts of sputum and numerous bacilli are not contraindications. The author feels that it is best to do a thoracoplasty at the start, especially in those in whom it is going to be difficult to secure regular refills for pneumothorax, which he was formerly accustomed to do routinely. He describes his technic and after-treatment in full. In only 1 case out of 37 has the author experienced an acute invasion of the sound lung, presumably from operation. Postoperative shock has been conspicuous by its absence. The two-stage operation has become routine. One death in 39 thoracoplasties was directly due to operation—cardiac failure on the twelfth day.

Carcinoma of the Colon.—ROMANIS (*Brit. Med. Jour.*, 1924, **183**, 3292) says the disease is both common and insidious. Early diagnosis is admittedly difficult. Uncomfortable sensations after meals and a certain amount of irregularity in action of bowels, either diarrhea or constipation occur. The right sided growths rarely cause constipation due to fluid character of stool and the difference in character of growth on the two sides. The site of growths is remarkably constant. Therefore the operations for removal have become well standardized. There are three types of growths encountered, the most malignant being the hard, craggy ulcer. The annular or ring type often met with on the left side and the fungating or palpable type are less malignant.

Urinary Antiseptics.—YOUNG (*Jour. Urol.*, 1924, **11**, 19) says that the best way of combating infections both general and local would be by intravenous injection of harmless chemicals. The author feels that the near future will find surgeons using this method for not only acute septicemias, otherwise fatal, but for serious chronic local infections, such as those encountered in the urinary tract. During the World War surgical results were transformed and thousands of lives saved by the progress made in the use of antiseptics. The advances in germicidal drugs since the war has been greater and has already transformed the therapy of infection in many specialties. The deep seated infections of the urinary tract are more difficult to cure but already much has been accomplished.

Experimental Closure of Large Bronchi.—BETTMAN (*Arch. Surg.*, 1924, **5**, 418) states that the pleura of the dog has a strong resistance to infection. His dogs died from pneumothorax. Lobectomy does not kill the dog. The animal survives the operation and within a short time is in as good health as before. The cut bronchus heals readily and firmly, but the healing is brought about by peribronchial tissue. The removal of an entire lung is technically easy. The dogs recover quickly from the operation, but almost invariably die in five days.

Operation Shock.—FRASER (*Brit. Jour. Surg.*, 1924, **11**, 410) remarks that operation on a case which shows persistent low blood-pressure should be delayed if possible until means have been taken to raise the blood-pressure. The operative procedure should be as short as is consistent with thoroughness. The least possible interference and trauma should be done. Every effort should be made to avoid unnecessary loss of blood. Chilling the patient before, during or after the operation must be avoided. If it is possible to exercise a choice of anesthetic, nitrous oxide and oxygen should be chosen. If simple restorative measures have failed to raise the blood-pressure, it should be raised by intravenous infusion of human blood, or 1 pint of 6 per cent gum acacia solution in normal saline. If examination of the blood shows that a condition of acidosis is present, a reserve alkali should be built up by the intravenous infusion of 1 pint of 4 per cent solution of sodium bicarbonate.

Case of a Retroperitoneal and Perinephric Infection (Abscess) Treated by Intravenous Injection of Mercurochrome.—YOUNG (*Johns Hopkins Hosp. Bull.*, 1924, **25**, 14) states that the remarkable results obtained with mercurochrome intravenously in septicemias prompted the author to use it in recent cases in which urethral and vesical instrumentation was followed by fever, gradually increasing pain and tenderness on left side reaching to the left kidney area. The detailed results record that a colorimetric method can be used to determine the strength in which mercurochrome after intravenous injection may appear in urine, stools and vomitus. A strength of 1 to 10,000 was maintained in the voided urine for three hours, and also in stools. The immediate sharp febrile reaction from the instrumentation followed by a rapid fall to normal and the disappearance of definite symptoms and signs of a retroperitoneal abscess from the mercurochrome injection seem

to verify previous animal experiments which show a pronounced general and local germicidal effect from intravenous injections of mercurochrome.

Diverticulum of the Urinary Bladder.—JUDD and SCHOLL (*Surg. Gynec. and Obstet.*, 1924, **38**, 14) claim that diverticula occur most commonly at the prostatic age, while the most common site of the outlet is in the region of the ureteral outlet. Diverticula were completely excised in 50 cases (series of 132 cases). Three patients died. In 37 cases in which there was obstruction of the vesical outlet, the diverticulum was excised and prostatectomy performed. In 46 cases the diverticulum was not removed. The ureter was involved in the diverticulum in 5 cases. In 20 cases the diverticula were associated with stones. Carcinoma occurred in the diverticulum in 4 cases. Three died shortly after operation, while the fourth lived sixteen months.

Knock-knee and Bow-leg.—SIMON (*New Orleans Med. and Surg. Jour.*, 1924, **76**, 329) says that knock-knee and bow-leg are by far the most common of deformities of the lower extremities, and comprise fully 15 per cent of all cases in Orthopedic Clinics. Bow-leg is the most frequent of the two, in most statistical records. Both deformities are more commonly found in the male than in the female child. At two periods of life do these two deformities most often develop, in early childhood, and in adolescence, when rapid growth may lessen the stability of supporting structures. Rickets is the basic etiology. The treatment of both conditions may be considered under three heads: Expectant or constitutional, mechanical, and operative. In bow-legs, the seat of operation is usually the tibia, in knock-knee, the fracture must be made in the femur above the condyles. Support for considerable periods is necessary.

Endothermy in the Treatment of Accessible Neoplastic Diseases.—WYETH (*Ann. Surg.*, 1924, **79**, 8) says that desiccation was devised and has been so brilliantly developed by Clark of Philadelphia. The desiccation spark is not hot enough to carbonize, but is of sufficient heat to cause rapid dehydration of the tissue, rupturing the cell capsule and converting the area treated into a dry mass. Moreover this method destroys tissue without opening blood or lymph channels and will act as a styptic when there is oozing of blood. It is impossible to overestimate the importance of the fact that with endothermy the growth is removed as a necrotic mass instead of as a group of viable cells. An important difference between endothermy and all other methods of cauterization by heat is that in endothermy the active electrode is cold when applied. Heat comes from within by the resistance of the tissues to the current. The three most important neoplastic tissues, tuberculosis, benign and malignant neoplasms, and syphilis all yield to this treatment. Cases are cited in full through article.

Brain Abscess with Pathological Observations.—BAGLEY (*Surg. Gynec. and Obst.*, 1924, **38**, 1) has arranged the avenues of infection in 4 groups: The extradural extension of the primary focus, with protrusion of the distended dura into the cranial cavity; secondary

invasion of the brain along the bloodvessels without extradural link; penetrating brain injury with infection by foreign body, deep, with or without stalk; abscess superficial and open, secondary to direct laceration and infection of the brain tissue. The author classifies the abscess walls as follows: Dense, fibrous, mesoblastic tissue wall; fairly firm wall containing some fibers proliferated from neighboring mesoblastic tissue; walls of varying thickness the result of glial proliferation; and walls showing no evidence of a protecting reaction. The clinical course of a brain abscess varies according to the infecting organism, the channel through which this organism reaches the brain, and the location of the infection in the brain substance as regards mesoblastic and epiblastic tissue.

Simple Ulcers of the Jejunum and Ileum.—BROWN (*Edin. Med. Jour.*, 1924, **31**, 45) says that simple ulcers are rare in these anatomical parts. It is, however, more frequent in the ileum than in the jejunum. The ulcers are rounded, clean-cut, with punched out edges, and tend to be terraced, the mucosa suffering more extensively from the necrotic process than the serous coat. It is not clear, however, whether the ulcer is primarily due to the elective localization of the bacteria or whether there is some alteration in the intestinal wall, which offers a suitable nidus for the organisms. The presence of gastric mucosa in abnormal situations has been offered as cause for such simple ulcers.

Carcinoma of the Papilla of Vater.—ABELL (*South. Med. Jour.*, 1924, **17**, 24) states that carcinoma of the papilla of Vater is usually slow of growth and late to give rise to metastasis, yet there are few situations where cancer so promptly gives evidence of its presence or so quickly devitalizes the patient. The author has had the unusual experience of 3 operative cases, which he analyzes at length. The first case lived for two years after the second operation. The terminal symptoms indicated obstruction of the duodenum, with metastases in the liver. The second patient is still alive three years and six months after operation, and four years after onset of symptoms. The lumen of the ampulla is so small that the growth causes symptoms almost coincidental with its appearance. Pancreatitis was present in these 3 cases, but they showed no glycosuria. Studies of the literature showed that transduodenal extirpation of the papilla was performed eighteen times, with 7 deaths and resection of the middle duodenum four times, with 2 deaths. Retroduodenal extirpation of the distal end of the choledochus, inclusive of the papilla three times, with 2 deaths. Excision of the papilla from the dilated choledochus through inversion once with operative recovery. It would appear that best results follow the radical removal in two stages: A preliminary cholecystenterostomy, with later transduodenal excision, suturing common duct mucosa to the intestine at point of division.

Studies on the Ureter and Bladder (with Especial Reference to Regurgitation of the Vesical Contents).—GRAVES and RAVIDOFF (*Jour. Urol.*, 1923, **10**, 135) state that regurgitation is an experimental fact. The conditions that favor its occurrence, however, have been less well understood and it is with these that the authors were particularly

concerned. In the case of normal rabbits it was found that ease of regurgitation depended upon many factors. The chief one among them was good bladder tone which seemed to be indispensable. It was learned that those bladders which were relatively empty and contracted at the beginning of the preparation produced reflex twice as frequently as those which had been recently distended with large amounts of urine. In the series in which the ureters had been rendered abnormal reflex occurred just as frequently as with normal structures and in cases where one ureter alone was distended the occurrence of regurgitation did not differ in its essentials on the two sides. The conclusion was therefore reached that the degree of ureteral activity has relatively little bearing upon regurgitation. The authors have never seen antiperistalsis in a normal ureter and in no way have they found it concerned in regurgitation. In spite of experimental difficulties reflex has occurred as a result of acute urinary obstruction. The authors have demonstrated that regurgitation of vesical contents into the ureter may be observed in the normal, intact, unanesthetized subject. Their final conclusion is that bladder regurgitation may be accountable for ascending infections of the urinary tract, particularly in cases of vesical neck obstruction.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,
OF PHILADELPHIA.

A Clinical Study of Rickets in the Breast-fed Infant.—DeBuys (*Am. Jour. Dis. Child.*, 1924, **27**, 149) in this series considered only those cases in which the symptoms were noted before complemental feedings were instituted. Cod-liver oil was not given in any case before there was unmistakable evidence of the existence of rickets. Lack of supervision and care seemed to cause the rickets to develop with more intensity. There was no noticeable increase in the symptoms after simple acute illness, but there seemed to be a direct relation between the severity of the rickets and the interval of non-supervision. There was no apparent relation between the severity of the rickets and the numerical order of the child in a family, or the number of children in a family. Syphilis was noted in only 8 instances as determined by clinical manifestations of the disease, and the Wassermann reaction. There was apparently no relation between syphilis and the severity of the rickets. The atmospheric conditions during the period of the study showed that the amount of sunshine was greater and the temperature higher than the normal average, and that the humidity was the normal average. According to the clinical manifestations of rickets, the disease was present in every case in the study. The disease was more marked in the colored subjects than in the white. There was no seasonal peak of the individual symptoms. There was a seasonal peak

of the combined symptoms noted in the month of March. Costal beading was the most frequent symptom. Enlarged epiphyses, cranial bosses, flaring ribs, and craniotabes followed in the order named. The short period of the existence of craniotabes, with its abrupt decline, was striking. Each symptom was more common in the colored than in the white. Beading showed the least difference. The difference increased as the frequency of the individual symptom decreased with the exception of craniotabes. Rickets should not be looked upon as a disease of the second half of the first year, but as a disease which may begin shortly after birth. In the study of the influence of rickets on the growth and development of the child it was seen that the heights of the white babies were normal average, but the heights of the colored babies were below normal average. The weights of the white babies were a little above the normal average. The weights of the colored babies varied so much for the different ages that they were too unsatisfactory for comparison. The weights of the markedly rachitic were below the normal average. While there was some slight variation in the measurements of the head, the most significant was the increased size of the head in the markedly rachitic colored babies. The chests of the colored babies were smaller than the average normal. The abdomens in this study were smaller than the normal average. In the markedly rachitic the abdomens were larger than the average normal. Tissue turgor was recorded as excellent only in the white. It was as poor more frequently in the white than in the colored. Dentition began earlier in the colored, and at the end of a year the average number for the colored was greater than for the white. Aside from the fact that the colored with the mildest rickets had more teeth and had them earlier, nothing was noted in the study as to the influence of the severity of rickets on dentition. A study of muscular development as reckoned by the ability to sit alone, stand alone and walk alone showed some slight variations between white and colored. It showed nothing between the least marked and the most marked cases of rickets.

A Study of Three Hundred Cases of Pertussis in a Hospital.—Herrman and Bell (*Arch. Pediat.*, 1924, **41**, 13) found that the females were more frequently affected with pertussis than the males. Eighty per cent of all cases of pertussis occur in children under five years of age. The largest number of cases of the disease occur during the summer months, at a time when the other communicable diseases are at their lowest ebb. Every spasmodic cough is not whooping-cough. There are cases of pseudopertussis. The term pertussis should be restricted to an acute infectious and communicable disease, caused by the Bordet-Gengou bacillus. Pertussis is most communicable in the catarrhal stage, when its true nature is not recognized. It is usually not communicable after the fourth week. In a series of 297 cases, the duration of the disease was from five to twelve weeks in 70 per cent of the cases. In 80 per cent the whoop lasted from one to four weeks, and in 86 per cent the vomiting lasted from one to four weeks. The Bordet-Gengou bacillus is regularly present in the catarrhal stage of the disease. The respiratory complications are by far the most important. They are present in 58 per cent of the series. Fourteen per cent had a complicating bronchopneumonia. The earliest and most characteristic change in

those patients who have bronchopneumonia is the presence of localized fine resonant rales at the base or at the angle of the scapula especially on the left side. The susceptibility and the unfavorable progress of pneumonia in infants is probably due to immunologic not to anatomical peculiarities. There is no conclusive evidence that pertussis is an important factor in the causation of tuberculosis of the lungs. A positive Pirquet reaction does not become negative in the course of the pertussis. The principal aids in the diagnosis of pertussis are the presence of a relative and absolute lymphocytosis in the blood; the presence of the Bordet-Gengou bacillus in the sputum and a positive complement-fixation test. The cutaneous tests have not proved of any value. The prognosis in pertussis depends on the age of the child and on the presence or absence of pulmonary complications. There are more deaths from pertussis among females than among males. Eighty per cent of all deaths from pertussis occur in children under two years of age. The greatest mortality occurs in the late winter and early spring, and is largely due to intercurrent catarrhal infections which cause pneumonia. In a series of 297 cases 90 per cent of the deaths were due to a complicating pneumonia. The mortality in those patients who had pneumonia was 18 per cent. The mortality in those who had pertussis and measles was 30 per cent. Pertussis is difficult to control because it is most communicable in the catarrhal stage, when its true nature is not recognized. In selected cases treatment in a hospital is necessary and advisable. The cough is not the only or the most important symptom of the disease. The nervous system and the nutrition are affected. Patients with this disease should be kept in bed. If possible the bed should be placed in the open air. Meteorological conditions seem to have an effect on the paroxysms, for patients may show changes in the frequency and the severity of the cough from day to day, irrespective of the treatment. In the control of the spasmodic cough, antipyrin fortified by the bromids has given the best results. The authors did not obtain favorable effects from injections of ether or from vaccination. Pertussis vaccine has a specific effect in about one-fourth of the cases. In those who fail to respond the vaccine may have been given too late, or the Bordet bacillus is not the cause. When a case of pertussis occurs in an institution for children an autogenous vaccine should be prepared and used for immunizing and treating.

Acute Infections of the Urinary Tract.— Pyelitis.—Hoppe (*Arch. Pediat.*, 1924, **41**, 29) says that this disease is not a clinical entity. Cystitis, ureteritis, calculi, pyelitis, pyelonephritis and renal abscess all give the same clinical findings by our present day clinical methods. Inflammation of the pelves themselves occurs in two forms, one of which involves the mucous membrane, and the other the submucosa and the peripelvic tissue. There are three routes of infection. It may ascend through the lumen of the ureter. It may ascend through the lymphatics around the ureters. The infection may be hematogenous, the bacteria localizing in the capillaries of the pelvic peripelvic tissues. The symptomatology is varied. Fever of obscure origin is most common. The diagnosis rests upon the finding of pus or bacteria in large quantities in the urine. Hexamethylenamin seldom gives good results in treating this condition. When it does act favorably it is probably

because the infection is chiefly in the bladder. The alkali group gives the most uniformly beneficial results. The sodium salt is best. The mode of action is not clear, but it is probably due to several factors such as diuresis, rendering the urine non-irritating and possibly the stimulation of leukocytic action and antibody formation. Foreign protein such as horse serum intramuscularly has been recommended in treating chronic cases. Vaccines are unreliable, but should be given a trial in obstinate cases.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.,

MAYO CLINIC, ROCHESTER, MINN.

The Wassermann Reaction in Diabetes.—ROCKWOOD and SANFORD (*Am. Jour. Syph.*, 1923, **7**, 679) report the results of Wassermann tests on 501 patients with diabetes, 201 by the Noguchi and 300 by the Kolmer technic. They conclude that there is only a coincidental relation between syphilis and diabetes in their series. False positives are rare in diabetes and do not exceed in number the proportion that would normally be expected as falsely positive in the types of technic employed by various authors.

The Roentgenotherapy of Pointed Condyloma.—SCHOENHOF (*Arch. f. Dermat. u. Syph.*, 1923, **142**, 380) directs attention to the superiority of roentgen-ray treatment over cautery and surgical ablation in the treatment of extensive and persistent condyloma formation about the genitalia, both in men and women. The report is based on 12 cases observed from six months to one year since cure. Papillomata within the urethral orifice and vagina responded, as well as those on the surface. It is necessary to employ a dosage just below the erythema limits and 3 to 4 mm. aluminum filtration with epilation in most cases, but no ill-effects were noted in any case. The relief afforded the foul vegetative cases is striking.

Syphilis in the Bechuana and Native.—MCARTHUR (*Brit. Jour. Dermat.*, 1923, **35**, 411) discusses the peculiarities of syphilis in the South African native, whose rapid syphilization is destined to provide a health problem of considerable magnitude for the future. The most notable points made by the author are: The absence of visceral lesion; the absence of neurosyphilides; the high incidence of tardive heredosyphilis; the chronicity of isolated lesions; "wit-kop," the favoid syphilide of the scalp. He remarks on Brock's observation that syphilitic fibrosis of the lung is exceptionally prevalent, and agrees with him as to its occurrence, although he finds it less common than Brock reports it (35 per cent). The author feels that syphilis markedly predisposes to tuberculosis among the natives. Neuro-

syphilis is unknown, and this exemption is by no means due to the absence of alcohol, as suggested in the case of the Arabs, for the Bechuana native is a heavy user of alcohol. Heredosyphilis is enormously prevalent and produces a marked reduction in physique. Hutchinsonian teeth are unknown, but mulberry molars take their place. In spite of the high incidence of familial syphilis, abortion and miscarriage are rare, and wholesale unrestricted marriage among infected and heredosyphilitic persons is the rule. The influence of physiological defence in recovery from syphilis is well illustrated by the response of many lesions simply to rest and feeding, without any attempt at specific treatment.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Treatment of Acute Salpingitis.—Most of the American gynecologists have assumed the attitude that the last word has been said in the matter of the treatment of acute salpingitis and for some years past they have been content to allow all of these cases to subside before considering the propriety of operative intervention. It will no doubt be somewhat of a surprise to the gynecologic surgeons on this side of the water to hear the views expressed at a symposium devoted to this subject in the section of Obstetrics and Gynecology of the 1923 meeting of the British Medical Association (*Brit. Med. Jour.*, September, 1923, p. 399). In the introductory paper, BOURNE advises operation at the earliest possible moment, that is, as soon as the disease is diagnosed as a suppurative salpingitis. At operation in this stage the tubes are greatly congested and plum-colored, with edematous fimbriæ and pus leaking from the abdominal ostium; plastic lymph adheres in flakes to the peritoneal surface of the tubes and neighboring viscera, such as the ovaries and uterus. Organized adhesions have not yet had time to form. Bourne states that each tube should first be slit up as far as possible along the border opposite to its mesenteric attachment, the pus very gently swabbed away, and the mucous membrane carefully inspected. Should it appear intact to the naked eye, only congested without ulceration or grayish patches of necrosis, the tube should be left *in situ* without any further treatment beyond a few sutures of thin catgut to fix the mucocutaneous surfaces at any point where there is arterial bleeding. Any cyst in the ovaries should be opened freely to prevent the formation of an ovarian abscess; a drainage tube is placed to the bottom

of the pouch of Douglas, and the abdomen is closed, or drainage may be provided through the vagina. The advantages which Bourne claims for laparotomy and salpingostomy are (1) that a check is given to spreading peritonitis and the formation of adhesions and peritoneal abscesses by opening and draining the pelvis; (2) the laying open of the tube drains its lumen and immediately offers it the chance of resolution without the risk of further permanent changes caused by a continuation of suppurative inflammation and (3) salpingostomy obviously renders the formation of a pyosalpinx impossible, and permanent thickening of the tubal wall extremely unlikely. If after laying open the tube, the mucous membrane shows gray patches of ulceration and gangrene it is beyond the power of functional recovery and should be removed. The only possible object of preserving the tubes is to maintain their function, and if this appears impossible owing to the extent of their destruction the tubes should be completely removed. By this operation there can be no further salpingitis, and the ovary is saved considerable risk of infection. To leave the tube alone and merely drain the pelvis is to invite the formation of chronic tubal disease and permanent ill health, with a long convalescence and possibly disturbed by residual abscesses. How far it is usual for so complete resolution to follow acute suppurative salpingitis with the crowning success of a subsequent pregnancy it is impossible to state for probably nobody has yet done sufficient operations of this kind, but cases are on record of pregnancy following salpingostomy of the tube in a chronic state and Bourne believes it is reasonable to expect similar success in the acute stage if operated upon early. If however, salpingostomy does fail to produce resolution and a functioning tube, no harm has been done by not removing the tube, since it cannot lead to a chronic pyosalpinx. At this meeting Bonney stated that for many years he had been an advocate of operating upon all cases of salpingitis at the earliest possible moment. It has been suggested that patients operated upon early have frequently to be reopened on account of collections of pus in the ovaries or pelvis, but he has never had to do this. While not denying that an inflamed tube may recover sufficiently to allow the occurrence of pregnancy, he is of the opinion that such complete recovery is rare. His experience with conservation with drainage has not been particularly encouraging. All of his cases recovered, but one nearly died of paralytic ileus, and none of them has conceived since the operation, while in 2 cases he had to reoperate on account of chronic disease of the appendages. The operation above described appeals to Bonney as being much more likely to lead to complete restoration of the tubal function, but one must remember that though it makes future closure of the abdominal ostium less likely, it can have but little effect on the uterine end of the tube. Early operation is exceedingly safe when the tubes are removed, and evidence seems to show that the risk is not greatly increased by conserving the tubes. He believes that a pyosalpinx or an ovarian abscess is a disgrace to the surgeon if the delay which allowed such formation is due to his advice. The parallel with appendicitis is a fair one. There the surgeon seeks to operate before abscess formation because the operation is safer than after an abscess has formed. In salpingitis also, the operation is safer before abscess formation, but in salpingitis there is an additional reason for early operation. No one wants to conserve an

appendix, healthy or unhealthy, but the ovary is a different matter, and now evidence is suggested that the tubes may be saved if operated on early enough. Natural cure of a pyosalpinx or an ovarian abscess is usually effected by adhesion to the pelvic colon with discharge of the pus into the bowel. Relief is not immediate as a rule, for there are generally two or more collections of pus and moreover the abscess cavity at once becomes analogous to a blind internal fistula with fecal infection of its walls and contents so that prolonged suppuration with intermittent discharges of pus anum is not uncommon. In delayed operations the surgeon frequently has to dislodge a tube or ovary which has already perforated into the bowel with the result that a fecal fistula up to the drainage tract develops within the first few days. This is an important objection to delayed operation and a valid reason in favor of surgical interference at the earliest possible moment. Finally, as a reason for immediate operation, there is always the possibility of faulty diagnosis. There are cases of pelvic appendicitis, diverticulitis and also early extrauterine gestation, which are impossible at the outset to distinguish from salpingitis. Continuing the discussion, BLAIR BELL stated that undoubtedly some mild cases of gonorrheal salpingitis recover spontaneously. In most cases however, he does not believe that the operation suggested will effect a cure since the interstitial portion of the tube will generally be occluded. Moreover, he doubts whether incision of the tube will lead to the disappearance of the organisms located in the mucosa which is a site of election. In answer to Bourne's proposal to perform salpingectomy to save the ovary from infection, he states that if a tube be enlarged and adherent it is extremely difficult to remove it without damaging the blood supply to the ovary. In such circumstances, when pregnancy is impossible, he performs ovarian grafting. PHILLIPS, in the concluding paper of the symposium, expressed the opinion that the tubes should be conserved, whether this be accomplished by medical treatment or by operation and slitting the tubes since even though the tubes are damaged by acute salpingitis, they still have a conceptional value. The closed ostial end can be reopened and the patency of the tubes established. He has performed reconstructive operations upon the tubes in 20 cases complaining of sterility and 5 of these (25 per cent) have become pregnant. The types of operations performed in these cases were (*a*) salpingostomy, (*b*) partial salpingectomy, (*c*) resection and anastomosis, (*d*) incision and resuture after canalization. It is hoped by the editor that the reader will understand the foregoing to be merely a report of the views of some of our British colleagues and by no means a personal endorsement. The subject is of considerable interest, although as yet largely theoretical, but further work in this field should be encouraged in suitable cases until sufficient evidence accumulates that its value may be truly estimated.

Results of Treatment of Bladder Tumors.—In reviewing 380 cases of vesical tumor YOUNG and SCOTT (*New York Med. Jour.*, 1923, **118**, 262) found that 80 per cent of bladder tumors occur between forty and sixty-nine years of age, being about equally distributed in these three decades. Both papillomata and carcinomata are much more frequent in the region of the trigone and ureteral orifices and adjacent lateral walls of the bladder and vesical neck. The anterior wall is less frequently involved and the vertex and upper posterior wall are much

more rarely involved. The vertex, anterior, upper lateral and posterior walls are most suitable for resection and excellent results may be expected by radical removal of a wide margin of bladder wall, while good results may be obtained by resection in the base of the bladder and region of the ureters. When the vesical neck is involved, deep cauterization is more effective than excision. Fulguration is the method of choice in benign papilloma, but in large tumors radium is of great assistance in causing a rapid disappearance of the tumor, and owing to the potential malignancy of all vesical papillomata, radium should generally be applied, if possible. In malignant papillomata, radium applied with an operative cystoscope and held in position with a clamp fastened to the table, is of first value and gives more brilliant results. Here again the conjoint use of fulguration and radium is advisable. The same treatment is sometimes completely effective in papillary carcinomata. Where the tumor is definitely malignant or very extensive, particularly if infiltrating, it should be attacked suprapubically, great care being taken not to touch the tumor or break off any papillary processes, and alcohol or 20 per cent resorcin applied to destroy any that may have dropped into the bladder or wound. If resection can be carried out successfully with a wide area of healthy bladder wall, whether extraperitoneal or transperitoneal or with transplantation of a ureter, it should usually be done, but the operation should not be so extravagantly extensive as to face a very high mortality rate. The position of radium implantation is still *sub judice*. A few brilliant and remarkable cases are reported and they have had some, but always associated with deep and widespread cauterization. Viewed as a whole however, the gloomy outlook which was held as to the curability of bladder tumors has passed. Fulguration, radium, the electrocautery and careful radical resection have transformed the situation, so that now about 95 per cent of the benign and 75 per cent of the malignant papillomata, about 50 per cent of the papillary carcinomata and somewhere near 25 per cent of the infiltrating carcinomata are probably curable by one or more of the methods above referred to. Young and Scott state there is no phase of surgery in which during the last ten years more gratifying advance has been made than in that of tumors of the bladder.

An Antiseptic Pyelographic Medium.—Although they were convinced that 12 per cent sodium iodide solution was the best pyelographic medium that had been suggested, CUNNINGHAM, GRAVES and DAVIS (*Jour. Urol.*, 1923, **10**, 255) deplored the fact that it had no antiseptic properties and they conducted an investigation to overcome this one drawback. After consideration of all possible antiseptics they decided the 1:3000 mercuric iodide in 12 per cent sodium iodide is the most satisfactory. They found that this solution has a phenol coefficient of 0.033 and when used in equal amounts with a colon bacillus infected urine, it destroyed bacterial growth in two and one-half minutes. They have employed it routinely in their clinic and have observed no immediate or subsequent ill-effects or discomfort, following its use either in the bladder or renal pelvis, even in the presence of acute inflammation. The addition of the antiseptic sacrifices in no degree the value of the medium from the standpoint of the roentgen-ray density. They believe that the use of this solution reduces to a minimum the risk of introduc-

ing infection and furthermore it provides some degree of positive benefit, apart from diagnosis, in cases in which infection already exists. The solution is prepared by dissolving 1 gm. of mercuric iodide in 3000 cc of 12 per cent sodium iodide. The latter is made with chemically pure sodium iodide and distilled water. The final solution does not need to be boiled.

Microscopical Compared with Clinical Diagnosis of Uterine Cancer.—Most investigators recognize the value of making a routine histological examination of all neoplastic tissue removed at operation but NORRIS (*Am. Jour. Obst. and Gynec.*, 1923, **5**, 1) has undertaken a study at the Laboratory of Gynecological Pathology of the University of Pennsylvania with a view to checking up with the actual figures the relative values of this procedure among the different types of malignant tumors. He found that cancer of the cervix can generally be diagnosed correctly by clinical methods since in his series of 253 specimens, 81.4 per cent were diagnosed positively by the clinician, 11.4 per cent were suspected and in only 2.3 per cent was malignancy unsuspected by the clinician. In contrast to this, of the 101 cases of fundal carcinoma that were studied, no fewer than 20 were clinically diagnosed as benign, 57 were positively diagnosed by clinical means, and an additional 24 were suspected of being malignant. Thus about 20 per cent were of the unsuspected variety, which in itself is sufficient evidence to prove the necessity for making routine histological examinations. Even after removal of the uterus, cases will be occasionally encountered that will prove puzzling until they are subjected to microscopical examination. Of the entire series of 101 cases of carcinoma of the fundus, curettings alone were submitted to the laboratory in 58 cases. Of these the clinical diagnosis was positive in 21 or 36.2 per cent, the clinical diagnosis was doubtful in 22 cases and in 15 cases (25.8 per cent), it was benign. Norris is unable to give the figures as regards the frequency with which the clinical diagnosis of malignant tumor was made but which proved to be benign, although he believes it a considerable group. Of 35 malignant connective-tissue tumors, only 8 appear to have been degenerations of previously benign neoplasms and since 1216 fibromyomata were removed during this time, the incidence of sarcomatous degeneration of myomata in this series was about 0.6 per cent. In confirmation of the correctness of the microscopical examination in the myomata and sarcomata it may be stated that follow-ups have been made on both and none of the myomata have had recurrences and over 80 per cent of the sarcomata have succumbed. The diagnosis of chorionepithelioma from the curettings alone is often impossible. Some specimens are so clearly malignant that a positive histological diagnosis is entirely justifiable, but many cases do not fall within this category. Norris states that this is appreciated by all gynecological pathologists, but is not fully recognized by clinicians at large. Summarizing the entire series of 391 cases of malignant tumors, it is found that the clinical diagnosis was correct in 272 cases (69.3 per cent); the true condition was suspected in an additional 59 cases (15 per cent); in 15 (3.8 per cent) the clinical diagnosis was of malignant tumor, but the type of neoplasm was not recognized, and in 45 (11.5 per cent) the condition was clinically regarded as benign and its true character determined only on histological examination.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA,

AND

DE WAYNE G. RICHEY, B.S., M.D.,

ASSISTANT PROFESSOR OF PATHOLOGY, UNIVERSITY OF PITTSBURGH; PITTSBURGH, PA.

The Influence of the Suprarenal Cortex on the Gonads of Rabbits.—I. THE EFFECTS OF SUPRARENAL INJURY (BY REMOVAL OR FREEZING) ON THE INTERSTITIAL CELLS OF THE OVARY.—As it is recognized that hypertrophic changes occur in the interstitial cells of the ovary, and in the suprarenal cortex, in certain animals during pregnancy, and, likewise that the removal of the gonads causes hypertrophy of the suprarenal cortex, JAFFE and MARINE (*Jour. Exper. Med.*, 1923, **38**, 93) conducted numerous experiments with the idea of ascertaining the effect which suprarenal injury might produce on the sex glands. Of the 30 rabbits which were subjected to double suprarenalectomy, a moderate or marked ovarian enlargement was observed in 76 per cent of those surviving the operation over thirty days. The ovarian enlargement consisted essentially of an hypertrophy of the interstitial cells. Twelve of the 13 rabbits, upon which a partial suprarenalectomy was performed, presented normal sized ovaries. The authors believe that "the hypertrophy of the interstitial cells is a compensatory reaction and adds further data to the functional interrelation between the suprarenal cortex and the interstitial cells."

II. THE EFFECTS OF SUPRARENAL INJURY (BY REMOVAL OR FREEZING) ON THE TUBULES AND INTERSTITIAL CELLS (LEYDIG) OF THE TESTES.—In a companion publication, the same investigators (*Jour. Exper. Med.*, 1923, **38**, 107) studied the effects of double suprarenalectomy on the testes of 48 rabbits and of partial suprarenalectomy on the tests of 45 rabbits. Contrary to the marked hypertrophy which occurred in the interstitial cells of the ovary, it was found that there were no specific changes either in the tubules or in the interstitial cells of the testes after double or partial suprarenalectomy. The authors state that "these facts indicate that the interstitial cells of the testes and ovary are not functionally homologous."

Diphtheritic Vaginitis in Children.—Having found 26 cases of diphtheritic vaginitis in children in searching the available literature for the last thirty years VAN SAUN (*Jour. Infect. Dis.*, 1923, **33**, 124) concluded that diphtheria of the genitals in children was uncommon and that primary genital diphtheria was rare, occurring only six times. The authoress reported a case, as developing in a girl of six years, who developed a membranous vaginitis thirty-seven days after a nasal culture yielded diphtheria bacilli. Although antitoxin was given and local treatment was instituted immediately, the child was very ill,

being unable to walk for three months. Positive cultures were obtained from the vulvar membrane for forty-two days, at the end of which time the diphtheria bacilli disappeared. About two months after the onset of the vaginitis, one positive throat culture was obtained. The organisms were found to be virulent and fermented dextrose. Since her recovery the child has remained in perfect health. In the cases collected from the literature, there were 4 deaths and the disease persisted from one to four weeks, as a rule.

Immunological Significance of Vitamins. Influence of the Lack of Vitamins on the Production of Specific Agglutinins, Precipitins, Hemolysins and Bacteriolysins in the Rat, Rabbit and Pigeon.—To determine the effect of a deficiency of vitamins A and B on the production of agglutinins, precipitins, hemolysins and bacteriolysins, WERKMAN (*Jour. Infect. Dis.*, 1923, **32**, 247) chose, as the animals for experimentation the rat and rabbit, because they are susceptible to a deficiency of vitamin A, and the pigeon, which is susceptible to the lack of vitamin B. Appropriate diets were used to produce xerophthalmia in the rats and rabbits and polished rice was given to the pigeons to cause polyneuritis, Bacillus typhosus served as an antigen in the production of agglutins, which were detected by a modified Dreyer technic. Human serum was used as antigen in the precipitin tests in the rats and Bacillus typhosus in the production of bacteriolysins in the rats and rabbits. Rabbit corpuscles were employed in the production of hemolysins in the rat and rat erythrocytes served as antigen in the rabbit. After divers controlled experiments with a large number of animals, it was found that rats and rabbits lacking vitamin A or B, showed no difference in their ability to produce agglutinins, precipitins, hemolysins or bacteriolysins. Pigeons, showing a deficiency of vitamin B, also were able to produce agglutinins. The author concludes that it is reasonable to believe "that cataphylaxis in animals suffering from the lack of vitamins is not the result of the destruction or paralysis of the antibody-forming mechanism that produces agglutinins, precipitins, hemolysins or bacteriolysins."

Influence of Lack of Vitamins on Resistance of Rat, Rabbit and Pigeon to Bacterial Infection.—Continuing his observations, WERKMAN (*Jour. Infect. Dis.*, 1923, **32**, 255) conducted a series of experiments to ascertain the influence of vitamins A and B on the natural resistance of the rat, rabbit and pigeon to infection. As both the rat and pigeon, and, but to a lesser extent, the rabbit, are normally immune to anthrax Bacillus anthracis was selected for inoculation, as well as a diplococcus resembling the pneumococcus, which was recovered from the lungs of a moribund rat. All experiments were controlled. The leukocytes and erythrocytes were counted independently. Blood platelets were determined by the Buckman and Hallisley method and the coagulation time of the blood was arrived at by use of the Brodie-Russel-Boggs coagulometer. During the course of the experiments, respiratory infections were noted in rats lacking vitamin A. In addition, 0.2 cc of a living eighteen-hour broth culture of Bacillus typhosus killed 3 of 4 rats lacking vitamin A, while none of the controls died. It was learned that rats and rabbits lacking vitamin A became less resistant to infection

with Bacillus anthracis and the pneumococcus, and that rats suffering from a deficiency for vitamin B also developed an increased susceptibility to these microörganisms. Moreover, pigeons fed on a diet lacking vitamin B only, and pigeons fed on a diet of polished rice, readily succumbed to infection with the anthrax bacillus and the pneumococcus, while the control pigeons survived. The results were similar to starvation susceptibility and indicated a marked break in resistance to infection.

Influence of the Lack of Vitamins on the Leukocytes and on Phagocytes.—In a third investigation, WERKMAN (*Jour. Infect. Dis.*, 1923, **32**, 263) determined the phagocytic activity in normal and immune rats and rabbits lacking vitamin A or B. The experiments were carried out *in vitro* and *in vivo*, employing the same strain of Bacillus typhosus. Leukocytes for the tests *in vitro*, were obtained from two or more stock animals by peptone injections and pooled. The method of Wright was used in the opsonic determination *in vitro*, while peritoneal washings from animals injected with 10 cc of an eighteen-hour culture of Bacillus typhosus supplied the material for the determination *in vivo*. In one experiment, Staphylococcus albus was used. It was found that the normal opsonic indices determined *in vitro* for Bacillus typhosus and Staphylococcus albus in rats and rabbits lacking vitamin A were not appreciably depressed. Similarly, the phagocytic indexes of rats lacking vitamin B for Bacillus typhosus did not exhibit marked variations from those of the control animals. A determination of the phagocytic indexes in immune rats *in vitro* likewise revealed no differences to account for vitamin cataphylaxis. The results *in vivo*, however, were somewhat more striking. The indexes were slightly greater in the rat in non-immunized controls than in non-immunized rats suffering from the lack of vitamin A or B. Similarly, in the immunized animals there was a consistent difference in favor of the control animals. These results appeared sufficient to be significant in vitamin cataphylaxis. The author states that "considered in the light of the results obtained *in vitro*, they suggest that the depression of the phagocytic activity does not result through a failure of the animal to elaborate opsonins, but as the result of a depressive agent acting on the phagocytic mechanism." He adds that "temperature may be of significance in this respect, as the body temperature is greatly lowered during vitamin starvation."

Chloride Retention in Experimental Hydronephrosis. — Having arrived at a method for producing experimental hydronephrosis which permitted the study of renal function in this condition for periods varying from weeks to months, and having learned that if the construction were removed within a week renal function was rapidly reëstablished, but ureteral obstruction of longer duration often led to permanent damage to the kidney, KEITH and PULFORD (*Jour. Exper. Med.*, 1923, **37**, 175) have increased the scope of their experiments. Selected, carefully controlled, female dogs were used. The dogs were allowed no food in short experiments. In the early experiments salt was administered by mouth in water, but later it was given subcutaneously, daily, in a concentration of about 1 per cent. Hydro-

nephrosis was produced by applying rubber bands about both ureters. The determinations used in the test of kidney function were: Phenolsulphonephthalein excretion by the test of Rowntree and Geraghty, urea of urine and whole blood by Marshall's method, chlorides of urine by Arnold's modification of Volhardt's method and chlorides of blood plasma by the methods of McLean and Van Slyke. It was found that in acute hydronephrosis, chloride retention occurred as well as retention of water, urea and phenolsulphonephthalein; that if both water and chlorides were retained there was no appreciable rise in the plasma chloride content; that when chlorides were retained, but not water, the chloride content of the plasma rose strikingly, and that, after removal of ureteral obstruction in acute hydronephrosis all renal functions may be rapidly restored in equal degree, or the chlorides may be retained temporarily, while there is free excretion of water and urea. In *chronic* hydronephrosis adequate daily excretion of urea and chlorides were able to be maintained by a compensatory polyuria. The authors conclude by saying that "chloride retention or an abnormal chloride excretion may occur in certain renal lesiens when there is no change in the urea, phenolsulphonephthalein or water excretion."

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Recurrent Serum Rashes.—Following a single injection of serum into the human body, an eruption frequently develops after a variable incubation period; it lasts a few hours or days and then disappears. Sometimes it recurs and a number of instances have been reported in which the rash was observed in two, three or even 4 distinct successive periods. It has been estimated that about 6 per cent of patients who develop serum rash have one or more recurrent attacks. These appear only when whole horse serum is used; following injections of refined antitoxin sera, pseudoglobulin, no recurrences were noted in Well's series of 9 cases or in the 129 reviewed by Coca. HOOKER (*Jour. Immunol.*, 1923, **8**, 469) reports recurrent rashes in a woman who was sensitized in 1897 with a small prophylactic injection of diphtheria antitoxin. In 1920 she was tested with normal horse serum by intradermal injection. In about twenty minutes an urticarial wheal developed which subsided in an hour; in five hours there recurred an itching wheal which disappeared in less than two hours; in twelve hours after

the test, for the third time, a wheal developed with redness which disappeared slowly. Later tests induced the same sequence of reactions. It was suggested by Goodall that the successive crops of serum rash represent separate reactions to sera, of different horses, which may have been pooled. This explanation is improbable because pooled pseudoglobulins have not been observed to produce recurrent attacks; because serum from one horse has produced recurrent endermal reactions; and because there is more convincing evidence that successive crops are the manifestations of successive appearances, at different time intervals, of sensitiveness to the different serum proteins—the explanation proposed by Dale and Hartley and substantiated statistically by Coca. There is ample evidence that euglobulin, pseudoglobulin and albumin are endowed with readily distinguishable antigenic properties. All of the recent investigations have disclosed the fact that the three proteins differ considerably in their antigenic "activities." These diminish with increasing solubility in ammonium sulphate solutions; euglobulin is the most active fraction, albumin the least active. Larger doses of albumin are necessary to sensitize and to shock guinea-pigs than is the case with euglobulin. The latent period before hypersensitiveness develops is appreciably longest with albumin. Incidentally, as Coca has shown, precipitin for egg globulin is produced earlier than for egg albumin. Davidson has recently conducted a detailed investigation of the various forms of serum rash and their relation to the proteins of whole horse serum. He recognizes three kinds of rash, urticarial, morbilliform and circinate; he considers that the diffuse erythematous type is probably due to scarlet fever. The average day of appearance of the rashes following injection is as follows: Urticarial, the ninth; morbilliform, the twelfth; circinate, the fourteenth. There being these three types of rash, and three dominant specific varieties of proteins in whole horse serum, Davidson concluded that each protein acts specifically in the human body to produce a certain type of rash. His correlation is as follows: Euglobulin produces the urticarial type because in experimental animals sensitiveness to euglobulin develops soonest, and because when concentrated serum is employed, with removal of euglobulin (and albumin) the urticaria is almost totally eliminated. The latter contention may be disputed; Park states that with regard to concentrated serum the later the development of the rash the more likely it is to be urticarial in nature. Sensitiveness to albumin develops latest and therefore probably causes the delayed type of circinate rash. Pseudoglobulin probably causes the morbilliform eruption. Thomson also reports that the circinate rash develops late and is more frequent after a previous urticaria. A triple reaction to horse serum has been shown by Hooker to be due to specific hypersensitiveness, to serum albumin, euglobulin and pseudoglobulin. Thereby, he believes the evidence that these proteins are severally and specifically concerned with the manifestations of recurrent serum is strengthened.

An Epidemiological Study of Folliculosis of the Conjunctiva.—Veldee (*Pub. Health Reports*, 1923, **38**, 2877) noted the difficulty of diagnosis of this condition, particularly in the differentiation from trachoma, and states that treatment and observation may be necessary

before a decision is arrived at. The rate among school children is much higher than has been reported for trachoma. The disease is most prevalent at five and six years having practically disappeared before twenty is reached. Social and economical conditions do not appear to be etiologically related. Size of family, sex, and nutritional conditions appear unimportant. Diseased tonsils appear to predispose to folliculosis. Errors of refraction have no marked influence. The concluding paragraph of this paper reads: "From the foregoing study of folliculosis it seems reasonable to conclude that it is an affection of early childhood, occurring somewhat more frequently in children with hypertrophied tonsils, developing no symptoms, running a very brief course as compared with trachoma, and disappearing spontaneously without sequelæ."

Diphtheric Vaginitis in Children.—VAN SAUN (*Jour. Infect. Dis.*, 1923, **33**, 124) states that a recapitulation of the cases of diphtheric vaginitis in children in the literature shows the relative infrequency as well as the rather indifferent reports of many of them. Primary diphtheria of the vagina is said to have occurred but 6 times in a series of 26 cases, and in some of these cases it is not quite clear but that a more extended examination might not have revealed another avenue of infection. Apparently, bacteriological examinations were made in 15 of the cases; virulence tests were made in but 6 of these. A number of the cases occurred in children physically below par. The mortality does not seem to have been higher in diphtheric vaginitis than in other forms of diphtheria. Four deaths were reported in the series collected. The duration of the disease would seem to have been anywhere from one to four weeks, as a rule. No mention is made of release cultures in any of the reported cases, although they may have been taken. The experience in the case reported by Van Saun indicates that they are quite as advisable after diphtheric vaginitis as after any other form of diphtheria infection. That several negative cultures obtained were followed by many positive cultures gives point to various articles on diphtheria carriers which have drawn attention to the well-known fact that two negative cultures are by no means conclusive evidence that the patient will remain free from diphtheria bacilli for even a short period of time.

The Elimination of Carbon Monoxide from Blood by Treatment with Air, with Oxygen, and with a Mixture of Carbon Dioxide and Oxygen.—SAYERS and YANT (*Pub. Health Rep.*, 1923, **38**, 2053) give the following summary of their paper:

1. Recovery from carbon-monoxide poisoning depends to a great extent upon early elimination of carbon monoxide from the blood.

2. The rate of elimination of carbon monoxide from the blood depends upon the percentage of oxygen in the air breathed, also upon the rate and depth of respiration.

3. Pure oxygen causes the elimination of carbon monoxide about four times as fast as normal air, when breathed by persons who have been gassed until 35 or 40 per cent of the hemoglobin in their blood has been combined with carbon monoxide.

4. Breathing a mixture of oxygen containing 8 to 10 per cent of carbon dioxide causes deep and rapid respiration.

5. Breathing a mixture of oxygen and carbon dioxide (8 to 10 per cent) causes the elimination of carbon monoxide about five to six times as fast as normal air, when breathed by persons who have been gassed until 30 to 40 per cent of their blood has been combined with carbon monoxide.

6. It is recommended that all victims not under a physician's care be caused to breathe oxygen in the purest form available for at least twenty to forty-five minutes.

7. It is recommended that physicians use the carbon dioxide oxygen mixture where possible, and note the results, but when the mixture is not available that they use pure oxygen.

Efficacy of Botulinus Antitoxin.—The Public Health Service (*Pub. Health Reports*, 1923, **38**, 2966) quotes from Hygienic Laboratory Bulletin No. 136 as follows: The discrepancies in the literature regarding the identification of the organisms concerned in the production of botulism and the isolation of a new type by the author prompted a more complete investigation of the so-called "botulinus" strains than has hitherto been attempted. The strains studied include representatives of different groups, particular attention being given to type C. The properties of toxin and antitoxin of organisms concerned in botulism are discussed at length, based on the author's experiments. As a result of these and prior investigations, an antitoxin has been elaborated and standardized. The author states that the curative effect of antitoxin in human cases has not been determined definitely, but that it seems reasonably certain that the antitoxin is effective prophylactically as is tetanus antitoxin. As to the effects produced when administered after symptoms develop, no certain statements can be made, owing to the fact that spontaneous recoveries of patients showing definite symptoms of botulism have been recorded. The curative properties are dependent upon the length of time elapsing between the consumption of the food and the administration of the antitoxin, and also on the amount of toxin which has been ingested. The most promising field for the use of the antitoxin is in outbreaks of botulism in which persons who have consumed food containing the toxin have not developed symptoms, or only slight symptoms. In any case, the use of antitoxin is indicated, since it is the only known specific remedy and the possibility always exists that the results may be favorable.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this* JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. JOHN H. MUSSER, JR., 262 S. 21st Street, Philadelphia, Pa., U. S. A.

Trademark Registered **STORM** Trademark Registered

Binder and Abdominal Supporter

(Patented)

Trade Mark Reg.

Trade Mark Reg.

For Men, Women and Children

For Ptosis, Hernia, Pregnancy, Obesity, Relaxed Sacro-iliac Articulations, Floating Kidney, High and Low Operations, etc.

Ask for 36-page Illustrated Folder
Mail orders filled at Philadelphia only—within 24 hours

Katherine L. Storm, M.D.

Originator, Patentee, Owner and Maker

1701 DIAMOND ST. PHILADELPHIA

D=Zerta

A Sugar=Free Dessert

FOR

Diabetic Conditions

WRITE TO

The Jell-O Company, Inc.

LE ROY, N. Y.

F. & R.'s
GENUINE
GLUTEN FLOUR

Guaranteed to comply in all respects to standard requirements of the U. S. Department of Agriculture.

Manufactured by
THE FARWELL & RHINES CO.
Watertown, N. Y., U. S. A.

Calcreose

In Bronchitis and Tuberculosis

Calcreose is particularly suitable as an adjunct to other remedial measures. **Calcreose** contains 50% creosote in combination with calcium. **Calcreose** has all the pharmacologic activity of creosote but is apparently free from untoward effects even when taken in large doses for long periods of time.

Sample 4 grain tablets supplied to physicians upon request

THE MALTBIE CHEMICAL CO., NEWARK, N. J.

THE STANDARD
LOESER'S INTRAVENOUS SOLUTIONS
CERTIFIED

Protect Yourself Against Substitution.

CERTIFIED

Loeser's Intravenous Solutions

CONTROL NO. **00403113**

THIS NUMBER IDENTIFIES THE INTRAVENOUS SOLUTIONS IN THIS PACKAGE AND CERTIFIES THAT THEY HAVE PROGRESSED THROUGH THE SCRUPULOUS LABORATORY ROUTINE OF THE LOESER METHOD.

RIGID CONTROL BY PHYSICAL, CHEMICAL AND ANIMAL TESTS INSURES THE ABSOLUTE ACCURACY AND UNIFORMITY REQUIRED FOR INTRAVENOUS INJECTION.

NEW YORK INTRAVENOUS LABORATORY
100 WEST 21ST STREET
NEW YORK

Look for the certificate on every box of the genuine solutions.

Logic That Leads to Starvation

YOU have a patient who has no tolerance for tomatoes. Another who has no tolerance for strawberries. Another who has no tolerance for milk or eggs or any one of a dozen or more foods.

Do you, on the evidence of these isolated cases of intolerance, issue a ukase to *all* your patients against these articles of food?

Ridiculous, you say! Why should you?

It *is* ridiculous, of course. You shouldn't! You should do just as you do—strike from the dietary of each patient the food or foods for which *he* shows intolerance or which may be specifically contra-indicated in his ailment. Any other course would eventually lead to starvation, because there is hardly a food for which someone does not show an idiosyncrasy.

But how about Coffee? Do you treat Coffee with the same respect? Most progressive practitioners do. No longer is Coffee, without therapeutic justification, swept from the dietary. The patient's normal routine is given consideration in case management.

Then, too, in Coffee you have at your instant command a mild but quick-acting stimulant which does not draw on the physical reserves of the body and which has no depressive after-effects, whereas *all other stimulants have!*

Coffee has diuretic properties; it is an aid to peristalsis; it is a first aid in exhaustion, and an antidote for certain poisons; and certainly your own nostrils tell you that it is an appetite excitant of rare power.

All these points have been firmly re-established by Samuel C. Prescott, Professor of Biology and Public Health at the Massachusetts Institute of Technology, Boston. Professor Prescott has just completed three years of Coffee research work, has read and digested over 700 articles, papers and books, mostly medical, and has brought out much information admitting of definite therapeutic application.

But outstanding above all the data are these two findings:

1. Coffee, the favored beverage of the American people, is, for "the overwhelming majority, a safe and desirable beverage."

2. Coffee offers itself as a close-at-hand therapeutic agent worthy not only of respect, but utilization.

Then why, in one broad dictum, ban Coffee without pathologic indications? Why, with thoughtless disregard, brush aside that which may be a normal remedy, and substitute drugs?

NOTE: *A summary of Professor Prescott's Coffee Research findings will be mailed to physicians on request.*

Joint Coffee Trade Publicity Committee, 64 Water Street, New York, N. Y.

Neosalvarsan

"The Dependable Original"

Made in the United States in strict conformity with Ehrlich's processes and formulas. Government tested.

Our obligation of responsible helpfulness towards practitioner and patient is being fulfilled through the medium of lowered prices of Neosalvarsan possible by quantity production.

I,	0.15 gram	$.60 per ampule
II,	0.3 "	.65 " "
III,	0.45 "	.70 " "
IV,	0.6 "	.80 " "
V,	0.75 "	.90 " "
VI,	0.9 "	1.00 " "

Neosalvarsan, the dependable original, is unsurpassed in low toxicity and is unequalled in therapeutic effectiveness. These facts have been demonstrated through extensive use during the past thirteen years and constitute a unique record.

Triple-glass-distilled water, in ampules, a proper solvent for intravenous medications.

Box of 5 ampules	10 cc. each	$1.00
" " "	20 cc. "	1.25

H·A·METZ LABORATORIES, INC.
122 HUDSON ST., NEW YORK

Calcium Absorption

Calcium glycerophosphate especially in the acid state, is unequalled for promoting calcium metabolism. It is rapidly absorbed and assimilated, and unlike calcium chloride does not cause gastric irritation on continued use.

ESKAY'S NEURO PHOSPHATES

contains calcium glycerophosphate in a peculiarly soluble and absorbable form.

SMITH, KLINE & FRENCH CO.
105 N. 5th St., Phila., Pa.
Established 1841
Manufacturers of
Eskay's Food

Leaves from a DIGITALIS NOTE BOOK

By. F. A. Upsher Smith, Ph. C.

No. VI

THE EMETIC ACTION *of* ACTIVE DIGITALIS

G. Canby Robinson states "The first requisite for the successful employment of digitalis is recognition of its toxic effect, especially of the early effects that serve as indications for discontinuance of the drug. Anorexia, nausea and vomiting are observed by all who use digitalis in sufficient doses; they are probably the commonest 'side-actions' encountered in the clinical use of digitalis bodies. Vomiting should be avoided if possible, especially in patients with severe symptoms of cardiac failure." Dr. Robinson in a later part of the paper says, "None of the preparations supposed to be devoid of effects on the gastro-intestinal tract should be used; the absence of this effect must be viewed as evidence of inactivity." (Medicine, May, 1922.)

Hatcher and Eggleston have shown that the gastric disturbances induced by digitalis are due to the action of the drug on the central nervous system and not on the gastric mucous membrane. (Journal Pharmacol. and Exper. Therap., 1912, 4, 113.)

As a grower of Digitalis, it is my opinion that in a carefully dried leaf there is but little decomposition, so that the active principles are at a maximum. The nauseating properties are inseparable from the active principles, and are a useful indication that the patient is becoming digitalized.

The Upsher Smith leaf, grown in Minnesota, where the activity of the leaf is high, is dried rapidly so as to retain its activity with a minimum of decomposition. Any nausea that may result may be attributed to the excellent potency of the leaf.

The Upsher Smith policy is to provide the medical profession with *active* products of his active digitalis, grown at Foxglove Farm. To this end, he offers it in two forms, standardized by the Hatcher cat method:

Capsules Folia-Digitalis (Upsher Smith), *1 gr. of the purified leaf or 1 cat unit in each. In bottles of 24, 500 and 1000 Capsules.*

Tincture Digitalis (Upsher Smith), *U. S. P. formula, one cat unit in ten minims. In one-ounce bottles only.*

Let us send you a trial package and arrange with your pharmacist and hospital to supply your patients with these active products of Foxglove Farm

Upsher Smith, Inc.
720 Washington Ave., S.E., Minneapolis, Minn.

Patients suffering with headache, drowsiness and twitching in the course of infections such as

SCARLET FEVER OR TYPHOID

may be alkalinized and often much relieved by feeding them a glass of

Kalak Water

every hour or two until the urine becomes neutral.

Each bottle carries in sparkling form several grammes of the bicarbonates of sodium, potassium, calcium and magnesium.

KALAK WATER COMPANY
6 Church Street,
New York City

For Relieving

Simple Insomnia

ADALIN

Has become the favorite remedy with many physicians, who value its safety and freedom from unpleasant by-effects. Where a ***Stronger Hypnotic*** is required

ADALIN-LUMINAL TABLETS
(Adalin 5 gr., Luminal ¼ gr.)

Meet the requirements without the need of powerful sleep-producing agents.

Both Adalin and Adalin-Luminal Tablets may also be used in small doses, several times daily, for the relief of ***Nervousness*** and ***Restlessness.***

How Supplied: ADALIN, 5 gr. tablets, tubes of 10 and bottles of 25; powder in ozs.
ADALIN-LUMINAL TABLETS, bottles of 25.

Literature on Request

WINTHROP CHEMICAL COMPANY, Inc., 117 Hudson Street, New York, N. Y.

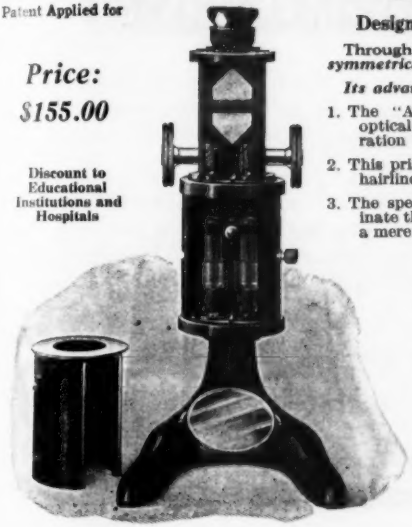
WINTHROP PRODUCTS
Conform to Original BAYER High Standards

LEITZ "BUERKER" COLORIMETER

Patent Applied for

Price:
$155.00

Discount to Educational Institutions and Hospitals



Write for Pamphlet No. L-1055

Designed after Suggestions of Prof. K. Buerker

Through the use of a new prism combination *perfectly symmetrical light rays* are obtained.

Its advantages are as follows:

1. The "Albrecht Huefner," prism renders symmetrical optical rays and prevents the appearance of color aberration within the optical system.
2. This prism divides the two comparison fields by a mere hairline.
3. The special containers for the deluent, practically eliminate the influence of the deluent and reduce the error to a mere minimum.
4. Clinicians, using this instrument, have easily been able to make readings *within an accuracy of 0.3 per cent.*
5. The construction resembles a microscope stand and is arranged in a most convenient manner, at the same time is small in dimensions.
6. Sliding metal doors close the entire colorimeter in an absolute light-tight manner.

60 East E. LEITZ INC. NEW YORK 10th St.

General Distributing Agents for Canada
THE J. F. HARTZ LTD., TORONTO, CANADA

Agents for Western States—California, Washington, Oregon, Idaho, Utah, Montana and Arizona:
SPINDLER and SAUPPÉ, 86 Third St., San Francisco, Cal.

Diabetes
Obesity—Restricted Diets
CELLU FLOUR

THE CHICAGO DIETETIC SUPPLY HOUSE INCORPORATED

Soy Bean Flour
Washed Bran
Agar-Agar
Mineral Oil
Gelatine
Sugar Free Flavors
India Gum
Cocoa Nibs
Cocoa Shells
Starch Free Baking Powder
Citric Acid
Food Charts
Gram Scales, etc.

The Chicago Dietetic Supply House, Inc.
1750-52 W. VAN BUREN ST. CHICAGO

Reliable Quality
Satisfactory Results

Horlick's Malted Milk

The Original

MANY USES

Write for literature on its use in insomnia, nervous, anaemic and digestive disorders, post-operative feeding, as an X-Ray meal, and other uses.

Avoid Imitations *Samples Prepaid*

HORLICK'S, Racine, Wis.

Convenient Aseptic

ASEPTIC AMPULES, S&D.

LABORATORY VIEW IN THE MAKING OF ASEPTIC AMPULES

Our Aseptic Ampules offer the physician a convenient, accurate and sterile method of administering certain medicaments either hypodermically or intravenously.

The care we exercise in the selection of the purest drugs and chemicals, also the aseptic precautions we employ in the making of our ampules, insure the physician of the best in this form of medication when prescribing Aseptic Ampules S. & D.

Our list of Ampules embraces everything for which there is an appreciable professional demand.

Sample supplied upon request.

SHARP & DOHME
BALTIMORE

New York Chicago New Orleans St. Louis Atlanta Philadelphia Kansas City San Francisco

An Invitation to Physicians

Physicians in good standing are cordially invited to visit the Battle Creek Sanitarium and Hospital at any time for observation and study, or for rest and treatment.

Special clinics for visiting physicians are conducted in connection with the Hospital, Dispensary and various laboratories.

Physicians in good standing are always welcome as guests, and accommodations for those who desire to make a prolonged stay are furnished at a moderate rate. No charge is made to physicians for regular medical examination or treatment. Special rates for treatment and medical attention are also granted dependent members of the physician's family.

An illustrated booklet telling of the Origin, Purposes and Methods of the institution, a copy of the current "MEDICAL BULLETIN," and announcements of clinics, will be sent free upon request.

THE BATTLE CREEK SANITARIUM Room 221 **Battle Creek, Michigan**

LIKE TAKING A POST-GRADUATE COURSE IN EUROPE

First American Edition

PHARMACOLOGY and THERAPEUTICS

By
E. POULSSON
Professor of Pharmacology, University of Christiana

English Edition Edited by
W. E. DIXON, F.R.S., M.D.
Cambridge University

This book is intended to give the practising physician knowledge of the best modern European practices in Pharmacology and Therapeutics. Not only is the pharmacology of the various drugs explained, but their practical therapeutic uses are clearly stated. The book is concise, yet comprehensive and thoroughly up-to-date.

Every physician and medical student will find this an invaluable reference book to have handy as a guide in determining the proper drug to indicate.

Possessing this book is practically equivalent to possessing the knowledge that might be gained in taking a post-graduate course in Pharmacology and Therapeutics in the best European schools, for it is used as a standard text in schools in England, Germany, Holland, Switzerland, Denmark, Sweden and Norway.

CLOTH, GOLD STAMPED, 519 PAGES, 6¼ x 9¼

Price, net, postpaid, $6.00

WILLIAMS & WILKINS COMPANY, Publishers of Scientific Books and Journals **Baltimore, Md., U.S.A.**

Rabies Vaccine—

The Factor of Safety

RABIES VACCINE (Cumming), P. D. & Co., contains no living virus. All risk of precipitating an attack of hydrophobia by the use of the vaccine is thereby obviated. With the original Pasteur preparation certain precautions must be observed if risk of infection is to be avoided.

The safety and efficiency of the Cumming modification of the original process has been amply demonstrated by its employment in over five thousand cases. Paralysis or other untoward result has never been observed following this treatment.

The sterility and safety of Rabies Vaccine, P. D. & Co., is secured by dialyzing a 1% suspension of rabic brain tissue (from rabbits dying of rabies induced by an injection of fixed virus) against running distilled water, the infectivity of the virus being thus destroyed without impairing the specific activity of the product.

The innocuousness of the finished material is then demonstrated by the injection of a given quantity beneath the dura of rabbits and subcutaneously in guinea pigs and mice. Sterility tests are likewise made, to insure freedom from bacteria. The product is standardized by weight so that 2 cc of suspension (the contents of one of the syringe containers) will contain sufficient material for one injection (one dose) for an adult.

Sterile and effective. Easy to use. No hospitalization or special equipment required. One injection a day for twenty-one days. On orders for the full course of treatment we ship immediately one package of seven doses and the other two packages at intervals of six days.

PARKE, DAVIS & COMPANY
DETROIT, MICHIGAN

Rabies Vaccine, P. D. & Co., is included in N. N. R. by the Council on Pharmacy and Chemistry of the A. M. A.

CHALFONTE-HADDON HALL

ATLANTIC CITY

Eight miles of Boardwalk, lined with a thousand and one fascinating shops and amusements. Eight miles of broad white beach and rolling surf. And, in the very center of things—on the Beach and the Boardwalk—hospitable, homelike Chalfonte-Haddon Hall. Their supreme appeal to people of culture and refinement extends over a period of more than fifty years.

In addition to Sea Bathing and Boardwalk activities:

GOLF
TENNIS
YACHTING
FISHING

American plan only. Always open.
Illustrated folder and rates on request.

LEEDS and LIPPINCOTT COMPANY

Hill—Manual of Proctology

THERE has been a crying need for a small, compact volume that will guide the general practitioner and surgeon in the recognition and treatment of rectal diseases. Encyclopedic treatises that historically follow the intensive studies in this special field are apt to weary the reader with excessive details. On the other hand the space devoted in general text-books is inadequate.

All controversial matter, irrelevant details, repetitions and references are omitted. Operations and methods that have not been proved of permanent value are excluded—*the only operations described in this work are the ones practised.*

The book is practical throughout—a working guide for the man in general practice and a valuable text for the student. Operative steps are carefully shown, but there is also much along medical lines—prescriptions, local applications, dietetic hints and on the important subject of after-treatment. Every paragraph is right to the point.

By T. CHITTENDEN HILL, M.D., F.R.C.S., Instructor in Proctology, Harvard Graduate School of Medicine; Surgeon to Rectal Department, Boston Dispensary, etc.

12mo, 279 pages with 84 engravings (mostly original)
Cloth, $3.25, net

Knowles—Diseases of the Skin

New (2d) Edition

PRACTICAL diagnostic tables have been added, showing the regional distribution of the common skin diseases and the types of lesions tending to involve certain areas. The sections on Roentgen-ray and Radium Therapy have been entirely rewritten. Food tests and other foreign protein tests are described with the method of application and the results obtained. This is a subject of considerable study today and of growing importance.

Bacterial and fungus origin of dermatological conditions are fully outlined. The section on ringworm fungi and eczematoid ringworm has been rewritten. Cancer of the skin is dealt with according to whether it originates from the prickle-cell or basal layer. The section on Syphilis has been greatly amplified and some forty new illustrations introduced.

By FRANK CROZER KNOWLES, M.D., Professor of Dermatology, Jefferson Medical College; Chief of Clinic, Dermatological Department, Pennsylvania Hospital, Phila.

Octavo, 595 pages with 229 illustrations and 14 plates
Cloth, $6.50, net

MEDICAL AND SANITARY

New (2d) Edition

Inspection of Schools

For the Health Officer, Physician, Nurse and Teacher

By S. W. NEWMAYER, A.B., M.D.

Formerly Chief of Division of Child Hygiene; Assistant Chief Medical Inspector, Bureau of Health; Supervisor of School Medical Inspection, Philadelphia

THE necessity of medical supervision of schools is now universally acknowledged. The previous edition of this book played no little part in this movement. The work is based on a personal experience of twenty-four years in this field and upon much intensive study of the highly organized systems and the methods employed in a great number of cities and towns. The good features from all have been included, so that this text actually represents the best practice of the day in each of the various activities of school health supervision. Let us emphasize that no "visionary ideals" are exploited, rather that the book deals with those methods which, in actual usage and practice, have proven to be the most successful. The book has been rewritten, greatly enlarged and contains a wealth of new material.

Part I. **Administration.**
Part II. **School Building and Grounds.**
Part III. **Communicable Diseases.**
Part IV. **Physical Defects.**
Part V. **Health of Teachers.**
Part VI. **Mentality.**
Part VII. **Allied Subjects of School Medical Supervision.**

12 mo, 462 pages, illustrated, with 79 engravings and 6 plates. Cloth, $4.00, net

---

BRAUN'S LOCAL ANESTHESIA

TRANSLATED AND EDITED BY

MALCOLM L. HARRIS, M.D.

PROFESSOR OF SURGERY, CHICAGO POLICLINIC; CHIEF SURGEON, ALEXIAN BROTHERS HOSPITAL; SURGEON TO THE HENROTIN, POLICLINIC AND PASSAVANT HOSPITALS, CHICAGO, ILL.

Octavo, 411 Pages, with 231 Illustrations in Black and Colors
New (6th) Edition. Cloth $5.00 Net

PROFESSOR BRAUN has justly been called "*the Father of Local Anesthesia*" and his book has been the standard on this subject since its first appearance. Nearly everyone who has written on the subject has drawn largely on the fund of information contained in this work. The *sixth edition* contains so much new matter and so much of the old has been rewritten that an entirely new translation was necessary. That so eminent an authority as Dr. Harris consented to edit the book adds much to its value.

Particular attention is called to the extensive revision of Chapter VI on Lumbar and Sacral Anesthesia and also to the additional material on Novocaine poisoning.

706-08 Sansom St. **LEA & FEBIGER** PHILADELPHIA

Just Off Press

MODERN UROLOGY

EDITED BY

HUGH CABOT, M.D.

DEAN AND PROFESSOR OF SURGERY, UNIVERSITY OF MICHIGAN

CONTENTS

GENERAL CONSIDERATIONS

Cystoscope; Methods of Diagnosis; Roentgen-ray Examination; Syphilis.

THE PENIS AND URETHRA

Anatomy, Anomalies and Injuries; Diseases of Penis; Genital Ulcers; Infections other than Tuberculosis; Diseases of Urethra in the Female, Stricture.

THE SCROTUM AND TESTICLE

Anatomy, Physiology, Malformations, Injuries and Torsion; Diseases of Scrotum; Hydrocele, Hematocele, Spermatocele and Varicocele; Infections of Testicle; Genital Tuberculosis; Tumors.

PROSTATE AND SEMINAL VESICLES

Anatomy, Physiology; Prostatic Obstructions; Cancer, Sarcoma and Calculus Disease of the Prostate.

THE BLADDER

Anatomy, Physiology; Malformations and Diverticulum; Injuries; Infections; Stone; Foreign Bodies; Tumors.

THE URETER

Anatomy, Abnormalities, Injuries and Diseases.

THE KIDNEY

Anatomy, Physiology; Functional Tests; Anomalies; Hydronephrosis, Movable Kidney, Injuries; Infections; Bilharziosis; Echinococcus; Tuberculosis; Stone; Tumors.

Contributors

J. DELLINGER BARNEY
B. S. BARRINGER
HORACE BINNEY
LEO BUERGER
HUGH CABOT
JOHN R. CAULK
B. C. CORBUS
H. A. FOWLER
JAMES A. GARDNER
JOHN T. GERAGHTY
FRANCIS R. HAGNER
PRESTON M. HICKEY
FRANK HINMAN
GUY L. HUNNER
EDWARD L. KEYES
HERMAN L. KRETSCHMER
BRANSFORD LEWIS
WILLIAM E. LOWER
RICHARD F. O'NEIL
ALFRED T. OSGOOD
WILLIAM C. QUINBY
HENRY L. SANFORD
GEORGE GILBERT SMITH
J. BENTLEY SQUIER
A. RAYMOND STEVENS
GEORGE W. WARREN
EDWARD L. YOUNG, JR.
HUGH HAMPTON YOUNG

New (2d) Edition

Cloth, per set, $18.00, net

Two octavo volumes totalling 1572 pages, illustrated with 686 engravings and 19 plates

706-08 Sansom St. **LEA & FEBIGER** PHILADELPHIA

INDEX TO ADVERTISERS

TO OUR SUBSCRIBERS—only ethical products of the highest quality can be advertised in this Journal. The firms listed below merit your full confidence, all are recognized leaders in their fields. Will you kindly mention THE JOURNAL when writing them? Thank you.

Apparatus and Instruments

(Colorimeters, Haemacytometers, Hemoglobinometers, Microscopes, Sterilizers, Bacteriological Supplies, etc.)

PAGE

Bausch & Lomb Co. 7
Castle, Wilmot, Co. 7
Hynson, Westcott & Dunning 20
E. Leitz, Inc. 27
Merck & Co. 16
Arthur H. Thomas Co. 3
Wilmot Castle Co. 7

Basal Metabolism Apparatus

Sanborn Company ..... 2d Cover
Arthur H. Thomas Co. 3

Binders, Supporters, etc.

Katherine L. Storm, M.D. 21

Blood Pressure Apparatus

W. A. Baum Co. 4
Becton, Dickinson & Co. 36
Sanborn Company ..... 2d Cover

Biologicals, Drugs and Pharmaceuticals

Abbott Laboratories 8
Arlington Chemical Co. 15
Armour & Co. 13
E. Bilhuber, Inc. 14
Calco Chemical Co. 5
G. W. Carnrick Co. 11
Ciba Co. ..... 4th Cover
Fairchild Bros. & Foster 5
Hoffmann-LaRoche Chemical Works 6
Hynson, Westcott & Dunning 20
Lavoris Chemical Co. 29
Lederle Antitoxin Laboratories 20
Eli Lilly & Co. 1
Maltbie Chemical Co. 21
Merck & Co. 16
H. A. Metz Laboratories 24
H. K. Mulford Co. 15
National Aniline & Chemical Co. 18
New York Intravenous Laboratory 22
Parke, Davis & Co. 30
Schering & Glatz, Inc. 19
Sharp & Dohme 28
F. A. Upsher Smith 25
Smith, Kline & French 24
Winthrop Chemical Co. 26

Electrical Diagnostic Instruments

Electro Surgical Instrument Co. 13

Electrocardiographs

Cambridge & Paul Instr. Co. 8

Foods, Beverages, etc.

Borcherdt Malt Extract Co. ..... 3d Cover
Célestin's Vichy 6
Chicago Dietetic Supply House 27
Corn Products Co. 9
Farwell & Rhines 21
The Fleischmann Co. 2
The Jell-O Co. 21
Horlick's Malted Milk Co. 27
Joint Coffee Trade 23
Laboratory Products Co. ....
Lister Bros., Inc. ..... 3d Cover
Mellin's Food Co. ..... 4th Cover

Acidophilus Milk

Cheplin Biological Laboratories 4
Lederle Antitoxin Laboratories 20

Malt Sugar

Borcherdt Malt Extract Co. ..... 3d Cover

Resorts and Hotels

Battle Creek Sanitarium 28
Chalfonte-Haddon Hall 31
The Homestead, Hot Springs, Va. 18
The "Spa," Waukesha, Wis. 8

Sutures and Ligatures

Armour & Co. 13
Davis & Geck, Inc. ..... 2d Cover

Syringes, Needles and Thermometers

Becton, Dickinson & Co. 36

X-Ray Apparatus, Tubes, etc.

Victor *X*-Ray Corp. 17

Miscellaneous

Dental Items of Interest Co. ....
Kalak Water Co. 26
Lea & Febiger 32–34
Williams & Wilkins Co. 29

B-D PRODUCTS

Made for the Profession

ASEPTO SYRINGE

No. 2043

No. 2043

Asepto Syringe outfit No. 2043 is especially designed for G-U patients and can be conveniently carried.

It insures safe, comfortable and sanitary administration of the prescribed medicine.

Write for literature describing the various styles and sizes of Asepto Syringes

SUPPLIED THROUGH DEALERS

BECTON, DICKINSON & CO.

RUTHERFORD, N. J.

Makers of Genuine Luer Syringes, Yale Quality Needles, **B-D** *Thermometers, Ace Bandages, Asepto Syringes, Sphygmomanometers and Spinal Manometers*

VOL. CLXVII,

AME
THE

E. B

CLINICOPATHOLO
LITIS. By C

THE ACCURACY O
HASKELL, M

PAROXYSMAL VE
DRED AND

CASE OF TRYPANO

SYPHILIS AS THE
OSTHEIMER
WINKELMA

A STUDY OF THE
BOARDMAN

THE VALUE OF PH
By LLOYD

CHRONIC APPEND

DISEASE OF THE

INDEX TO ADVE

Philadelphia

COPYRIGHT, 1898, BY LEA

PUBLISHED

S

GE

043 is
tients
ied.

e and
e pre-

styles

O.

rmometers,
lanometers